Review

Integrative Chronic Pain Management: A Narrative Review

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Review

Integrative Chronic Pain Management: A Narrative Review

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Abstract: Many people in the USA have lost their lives or become addicted to opioids via prescription opioids given for chronic pain. The chronic pain epidemic has emerged due to a convergence of factors, including the medicalization of pain as well as injuries happening in the workplace, in the home, or during recreation. Opioid prescriptions rose precipitously from the late 1990's through to approximately 2020, and despite public awareness, still are increasing. This review examines literature on integrative approaches to chronic pain as delineated by pain type. The review is organized by the most common causes of chronic pain, and randomized controlled trials, meta-analyses and systematic reviews are extracted for each cause of chronic pain. Several promising interventions may alleviate chronic pain of some causes, and some interventions may work across pain causes. Lowering inflammation through dietary or lifestyle regimens may be a general way of reducing pain. Pain can be alleviated through several adjunctive and integrative treatment approaches, which may serve to lower the need for opioid medication.

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Introduction: The Epidemic of Chronic Pain

The opioid crisis in the United States underscores a complex convergence of factors, with 91,799 deaths attributed to drug overdoses in 2020 [1]. Notably, drug overdoses surpass auto accidents and gun deaths as a leading cause of death in young men [2]. This crisis disproportionately affects post-industrial regions of the US, where employment opportunities have dwindled [3]. Chronic pain affects a staggering 126.1 million Americans within a three-month period, with 25.3 million experiencing daily pain [4]. Alarmingly, two-thirds of chronic pain sufferers in 2019 continued to experience chronic pain in 2020 [5].

Chronic pain prevalence is highly age stratified [6]. Individuals above 75 years old in the UK experience chronic pain rates between 46% and 62%, compared to rates of 31% to 32% among those aged 25 to 34 [7,8].

Chronic pain profoundly impacts employment, with sufferers being more likely to be unemployed [9]. Moreover, navigating work with chronic pain proves challenging and often limiting [10]. Fifteen percent of chronic pain patients experience high-impact chronic pain, severely constraining their activities [11]. This limitation translates into 3.7 times more missed workdays compared to those without chronic pain [11].

Demographic factors further influence chronic pain prevalence. Native Americans and multiracial adults exhibit the highest pain prevalence, while Asian Americans report the lowest rates [12]. 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 [13]. Notably, two-thirds of adults with chronic pain have comorbid psychiatric diagnoses [14].

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Chronic pain remains a pervasive issue, with one in nine young adults in the US affected [15]. Women, older individuals, Caucasians, and non-Hispanic populations are at increased risk of chronic pain [16].

Opioid prescriptions for chronic non-malignant pain pose risks, with 3.3% of chronic pain patients developing abuse or addiction behaviors [17]. Effective management of chronic pain requires a multifaceted approach aimed at prevention and providing support for those grappling with opioid use disorders (OUDs). Other adverse effects of opioid use to treat chronic pain is the well know fact that opiates increase the incidence and recurrence of cancer [18].

In the whole USA, opioid deaths are 3.2x higher in 2016 than 1999[1] and opioids are responsible for 2/3 of drug overdose deaths [19]. Chronic pain is a massive drain of resources, as chronic pain patients visit clinics at 3.4 times the rate of the general population [20], and pain complaints comprise 40 to 50% of primary care consultations [21]. 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 considered[22].

Apart from fatalities, opioid addiction engenders numerous harms, including criminal activities driven by the need to procure opioids [23] . Volumes of illegal opiates entering Canada and the USA have greatly increased since 2019 [24] and are used in the majority of overdose deaths.

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.

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. Chronic pain has many sources, as included in Table 1 below. Table 1 below summarizes the main contributors to chronic pain, 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).

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 in patient population	Opioid abuse prevalence in opioid using population
Rheumatoid Arthritis	0.6% [25]	Smoking[26] Latin American Indigenous background [27] Female [28]	85% [29]	25% using opioids every month throughout duration of 7 year study [29]
Injuries	13%[†] [30]	Male [31] Occupational danger exposure [32] Young age (rate of injury) [33] Old age (injury severity) [33]	27% to 6% [34]	16% [35]
Low Back Pain	33% [36]	Female,	42% [38]	43% [39]

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		Obesity, Smoking, Strenuous Work, Sedentary Transport [37]		
Post-surgical pain	8%‡ [40]	Genetic factors, Psychological disposition, Young age [41]	37% [42]	26%[43]
Cancer pain	0.1%** [44]	Young age [45], Obesity, Education, chemotherapy, hormone therapy [46]	35% of cancer patients [47]	19% [48]
Fibromyalgia	3% [49] to 5% [50]	Female[49]	14% [51], 22%[52], 32% [53]	39% [54,55] to 45% use opioids after 1 year
Bowel Pain	13%[56]	Younger age [56]	13% [57]	23% to 38%* [57]
Headaches and Migraines	12%[58] to 16% [59]	Female [59]	30% [60]	17% (for dependence) [60]
Neuropathy	7% to 8% [61,62]	Older age, Female, Manual occupation and social deprivation [63]	7% [64]	3%-19% (General chronic pain population) [65]

* Based off a 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 [57]. †Nepalese survey, which may be nonrepresentative [30]. ‡Based on a 24% three-year prevalence of surgery [40]. ** Based on 1.5% five year incidence of cancer [44] and chronic pain in 40% of cancer patients.

Identifying the sources of chronic pain presents challenges, with post-surgical patients experiencing chronic pain one year after surgery at rates up to 12% [66]. Arthritis and back problems emerge as leading causes of chronic pain, with arthritis affecting 48% and back problems 29% of chronic pain patients, respectively [67]. Additionally, other conditions contribute to chronic pain in 28% of respondents, with over 10% reporting multiple causal conditions [67]. 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 [68].

In the UK, chronic pain rates rose from 41% in the 1990s to 45% between 2010 and 2015 [6]. 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% [69]. Approximately 50.2 million US adults, or 20.5% of the adult population, experience pain on most or every day [70].

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 are included in Table 1.

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Before examining the specific causes of chronic pain, we first examine interventions which 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 reducing pain levels [71].

Another meta-analysis of ketogenic diets and their impact on neurological and inflammatory outcomes summarized the impacts of ketogenic diets on neurological outcomes [72]. 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 demonstrate significant reductions in pain [73].

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 [74].

Of the five trials for caloric restriction and/or fasting, all showed an improvement on pain symptoms [75–79]. It should be noted that for two of these trials, the impact on pain may have been mediated by weight loss causing less stress on the knee joints [76,78], and one trial was using specialized, low in fermentable oligo-, di- or mono-saccharides and polyols (low FODMAP) diet, albeit calorie consumption was reduced in the treatment group [79]. Sources of pain in these trials varied, from migraine[75], knee joint pain[76,78], fibromyalgia[77] and gastro-intestinal [79], so fasting and caloric restriction for pain treatment may be less useful for generalized pain treatment.

Two trials covered enriched polyunsaturated fatty acid diets which were for the treatment of headaches[80,81]. Patient pain improved in the Ramsden et al. 2013 trial of 67 subjects experiencing daily headaches [80], and migraine headaches became less frequent in the Soares et al. 2018 trial of 51 subjects [81]. 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 [82]. Omega3 FA tend to reduce inflammation and pain via the arachidonic acid pathway [83]. Specialized pro-resolving mediators (SPMs) can be even more effective at resolving inflammation and pain[84,85].

While seemingly contradictory, low fat plant based diets were also successful at reducing patient pain scores for pain from diabetic neuropathy [86], migraines [87], fibromyalgia[88], non-alcoholic mild pancreatic disease [89], and musculoskeletal pain [90]. One double-blind randomized control trial (RCT) of a high protein diet showed substantial improvement in chronic back pain[91].

Gluten elimination showed beneficial improvements in fibromyalgia patients[92,93]. Elimination of monosodium glutamate (MSG) improved symptoms in patients with irritable bowel syndrome (IBS) and fibromyalgia [94], whereas another study of fibromyalgia (but not IBS) patients did not show improvement when MSG and aspartame were eliminated [95]. Restriction of lactose improved abdominal pain in lactose intolerant individuals [96,97], though this result may be considered trivial.

Antioxidant-rich diets improved pain or quality of life in several trials [98–106] included in the 2020 review by Dragon et al. [74]. The agents studied varied, from separate formulations including many different anti-oxidant components, which improved migraine pain [100] and abdominal pain in chronic pancreatitis [99]. One study of a custom anti-oxidant formulation, including vitamin D3 on musculoskeletal pain due to breast cancer showed no change in musculoskeletal symptoms [103]. Vitamin D2 was effective at lowering musculoskeletal pain levels in breast cancer due to chemotherapy [104]. In Vitamin D-deficient patients with chronic low back pain, Vitamin D3 supplementation improved function and lowered pain intensity [98,102]. Vitamin D3 supplementation also decreased migraine frequency in a double-blind RCT of 48 subjects [101]. 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 [105].

Dietary interventions increasing the fruit and fiber content of patient diets were successful at reducing musculoskeletal [107,108] and bowel pain [109,110]. For abdominal pain, probiotic

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supplementation improved pain scores [111–113].Patients with neck and shoulder stiffness and headaches saw some pain alleviation with probiotic supplementation [114]. However, one study of fibromyalgia patients given a probiotic supplement did not show improvement [115].

Botanicals, including curcumin and Boswellia serrata are effective for pain relief[116–118]. Ginger[119] and other herbs[120–124] may have benefit in the adjunctive setting.

More equivocal, albeit positive results exist for photobiomodulation (PBM) therapy on post-surgical pain [125]. Mouse models show a significant reduction in inflammatory pain using red LED light[126], and another mouse study demonstrated reductions in pain sensitivity after photobiomodulation using 808nm wavelength light [127]. One human trial of PBM demonstrated a reduction in the inflammatory biomarker prostaglandin E_2, but no reduction in pain levels after PBM [128]. Another meta-analysis from the same group shows non-clinically significant reductions in pain [129]. However, when an adequate dose of PBM therapy showed improvement when given as part of a regimen including exercise, when compared to exercise alone [129]. Moxibustion may improve chronic pain, and can even be self-administered [130].

The next section of this manuscript focus on the specific causes of pain and their integrative treatment, including arthritis, musculoskeletal pain (injuries, post-surgical 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 also can help lower pain severity [131–133].

Arthritis

As mentioned before, arthritis is the most common cause of chronic pain, responsible for pain in 48% of chronic pain patients [67]. Interventions to address arthritis can decrease reliance on opioids for pain management. Forty percent of rheumatoid arthritis patients use opioids regularly [134,135], and opioid users often have worse physical outcomes [136,137].

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 [73,138]
Traditional Chinese Medicine	Reduction in tender joint count [139]
Combination electroacupuncture, moxibustion and massage	Reduction in pain [140]
Tripterygium wilfordii Hook. F combined with methotrexate	Combination was superior to methotrexate in isolation [141]
Omega-3 fatty acids	Reduction in non-steroidal anti-inflammatory (NSAID) medication and tender joint count [142] Favorable effect [143]
Fasting	Improvement in symptoms compared to control group when combined with a vegetarian diet [144,145]
Cat's Claw	Some benefit [146]
Mediterranean diet	Improvement [147]
Ginger	Improvement [148]
Feverfew	Grip strength improvement [149]

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Musculoskeletal Pain, Post-Surgical 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[150]. In a study of 76 men and 83 women (149 subjects overall) experiencing spinal pain, 53% used opiates [151].

Opioid use in musculoskeletal pain often results in the persistence and enhancement of chronic musculoskeletal pain, as pain signals are upregulated (hyperalgesia) [152]. Use of opioids often negatively impacts the treatment outcomes in low back pain [153]. Chronic pain prevalence after spinal cord injury is 68% [154].

General pain declined after the use of the emotional freedom technique (EFT), which involves tapping acupressure points [155].

Injuries

While injuries are as varied as the stories leading into them, and it is difficult to talk about statistical aggregates about injuries. Prevalence of prolonged opioid use after musculoskeletal injury ranges between 27% for patients with high rates of prior substance use disorder to 6% for low-risk populations[34]. A separate survey found a 4% opioid abuse rate in users with no prior history of opioid use [156]. This is similar to other estimates of 3% [35]. For workplace injuries, 16% of people prescribed opioids were still using opioids one year later, with increasing doses on average [157].

Opioids can increase the risk of falls and associated injuries, contributing possibly to a self-reinforcing cycle [158]. 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 [159]
Massage	Improvement in pain levels [160]

Post-Surgical

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 narcotics [161]. 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 [162].

More accurate data has since been collected; in a Canadian study, the rates of opioid use 1 year post-operation were 0.4% [163]. Rates for opioid use 90 days post surgery are 3.1% [163]. A meta-analysis calculated 7% of patients using opioids more than 3 months after surgery[164], consistent with another estimate of 6% to 7% [165].

Alternatives to reduce opioid use for post-surgical pain are included in Table 4 below [166–168]. Acupuncture, among other interventions, is promising in reducing post-operative pain[169].

Table 4. Interventions to treat post-operative pain.

Intervention	Effect
Acupuncture	Reduced post-operative pain [169]
Complementary and Integrative Methods	Management of Postoperative Pain [167]
Guided imagery	Improved pain [170]
Integrative medicine	Reduce pain and increase quality of life [171]
Relaxation therapy	Reduced pain [172]
Integrative Korean Medicine	Reduced the incidence of post operative pain [173]

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Back Pain

Back pain is a prevalent concern, with 33% of those consulting primary care physicians receiving opioid prescriptions [174], while short-term opioid use stands at 22% [175]. However, opioids offer minimal relief for low back pain (LBP) [176].

Prevention emerges as a crucial strategy for addressing LBP. Exercise coupled with education reduces the risk of LBP episodes by 45%, while exercise alone diminishes episodes by 35% [177]. Various meta-analyses underscore the combined preventative impact of exercise and education [178,179]. Conversely, product-based interventions like back belts and shoe insoles exhibit limited or no effectiveness in preventing LBP [177].

Several risk factors contribute to LBP, including obesity [180], sports participation [180], and lifting heavy loads exceeding 25lbs [181,182]. Office workers exhibit the highest prevalence of LBP according to a German survey [183]. Strengthening lower limb muscles emerges as a protective measure against LBP [184,185]. Notably, a 3 days/week strength training program reduces one-year recurrence rates to 8.3%, representing a 75% reduction compared to the control group [36].

Complementary interventions offer promising avenues for managing LBP. Yoga demonstrates a positive impact on long-term LBP reduction[186], while evidence regarding medical cannabis remains of low quality, necessitating further investigation [187,188]. Psychological approaches such as cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR) yield improvements in LBP [189]. Lessons in the Alexander Technique[190], focusing on posture coaching, effectively decrease LBP incidence [191,192].

Although with lower confidence, modalities like massage [193], spinal manipulation, and transcutaneous electrical stimulation show potential in reducing LBP [194]. Acupuncture also presents a favorable effect [193].

Additionally, dietary interventions offer avenues for managing chronic back pain. A double-blind randomized control trial (RCT) reveals substantial improvement with a high-protein diet [91]. Weight loss through dieting and adopting low-inflammatory diets can alleviate LBP [195,196]. Conversely, alcohol consumption may exacerbate LBP [197].

Integrative approaches for LBP can reduce the need for opioid medications. Interventions for treating LBP are summarized below in Table 5 [198].

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

Intervention	Effect
Integrative treatment	Improvement in pain and enhance quality of life [199,200]
Spinal manipulative therapy	Improvement in low back pain [201]
Chiropractic and integrative care	Pain reduction [202]
Yoga	Reducing long-term lower back pain [186,203,204]
Cognitive behavioural therapy (CBT) and mindfulness	Stress reduction can improve LBP [189]
Alexander Technique	Reduced the incidence of LBP [191,205]
Massage	Reduced pain [206]
Dieting	Weight loss can reduce Lower back pain [196]
Spinal manipulation and transcutaneous electrical stimulation	Reduced pain [207]
Acupuncture	Positive impact [206]
Theramine (amino acid supplement)	Positive impact [91]

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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 2.5million cancer survivors in the USA respectively [208]. Pain prevalence varies based on the cancer stage and treatment stage. After treatment, pain prevalence is 39%, and is 55% during anticancer treatment and 66% in advanced, metastatic, or terminal disease[209].

The prevalence of opioid use disorder in those with cancer related chronic pain is 8%, and the risk of use disorder is 24% [210]. There is a pressing need to reduce the need for opioids, as opioids can increase the risk of cancer [18]. Interventions for treating cancer pain are available in Table 6 [211–213].

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[214–216]
Yoga	Reduction in cancer pain [165–167]
Guided imaginary and PMR	Reduction in general cancer pain [220,221]
Reflexology	Reduction in general cancer pain [222–226]
Massage	Reduction in general cancer pain [227,228] and pain during palliative care [229,230]
Electrical nerve stimulation	Trend for efficacy in patients with cancer pain [231]
Hypnosis	Benefit on pain relief for advanced breast cancer [232,233]
Laxation, meditation, imagery, music therapy, virtual reality	Relieved depression, stress, anxiety, and other mood disturbances associated with pain [234,235]
Education and communication	Improvement in quality of life [168]
NMDA Antagonists	Improved management of neuropathic pain [236]
Cannabis	Improved management of cancer pain [237]
Tetrodotoxin	Treatment of uncontrolled moderate to severe cancer-related pain [238]
Botulinum Toxin Type A (BoNT-A)	Improvement in nociceptive and neuropathic cancer pain[239,240]
TRPM8 Activator Menthol	Improvement in localized cancer-related neuropathic pain [241]
Growth Factors Inhibitors	Decreased metastatic cancer-related bone pain [242]
Lemairamin	Antinociceptive effects in pain hypersensitivity [243]
Physical exercise	Positive impact on pain when combined with cognitive-behavioral therapies (CBT) or lifestyle programs [244,245]
Emotional dimension (Supportive-expressive group therapy Music therapy)	Improved cancer pain scores [246]
Mindfulness mediation	Positive effects on some chronic pain conditions [247]

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Fibromyalgia

Fibromyalgia is characterized by widespread body pain, and affects roughly 5% of the US adult population[50]. It affects women significantly more often than men, and the ratio of women to men with fibromyalgia is at least 2.3 to 1, depending on diagnostic criteria[50]. Of patients with diagnosed fibromyalgia, 31% used opioids regularly or at high doses, while 27% used opioids intermittently or at lower doses[248]. Forty two percent reported minimal or no use of opioids, leaving 58% of fibromyalgia patients using opioids to treat their pain.

One survey found 32% of those referred to a fibromyalgia clinic used opioids [53], despite limited evidence for efficacy benefits outweighing risks [249].

Interventions for FM are included in the below table (Table 7) [250].

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 [251]
Heart Rate Variability Biofeedback	Related to decreased pain [252]
Mindfulness	Contribute to symptom management in chronic pain conditions [253]
Education + Cognitive Behavioral Therapy	Improvement in patient pain [254]
Pilates	Beneficial effects on pain and quality of life of individuals [255]
Pain Neuroscience Education, Exercise Therapy, Psychological Support, and Nature Exposure	Improvement in affective valence, arousal, dominance, fatigue, pain, stress, and self-efficacy [256]
Photobiomodulation	Treat chronic pain syndromes [257]
Exercise and Massage	Improvement in pain and other symptoms [250]

Bowel Pain

Of those with inflammatory bowel disease (IBD) presenting to a clinic, 13% used opiates [57]. Additionally, 3% of IBD patients and 5% of Crohn's disease (CD) patients were addicted to narcotics [57]. One estimate from 1988 found that 30% of IBD patients referred for psychiatric consultation were addicted to narcotics [258].

Bowel pain may be the result of specific intolerances, including gluten sensitivity or celiac disease[259], lactose intolerance [260].

Interventions and their studied effects are available in (Table 8) [261,262].

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 [263]
Antibiotics, probiotics, prebiotics, postbiotics, synbiotics, and fecal microbiota transplantation	Improvement of Intestinal Microecology [262]
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 [264]

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Exosome Therapy	Maintaining intestinal barrier function [265]
Diet (diet of low-FODMAP)	Symptom relief and improvement of life quality [266,267]
Mood and Psychology training	Reduction in recurrence of the disease [262]

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 [268]. Migraines are estimated to affect 12%[58] to 16% [59] of the general population. Migraines are more common in younger people, women, and people with lower socioeconomic status [59]. Over one quarter of women aged 18 to 54 years experience a severe migraine or headache in the past three months, compared to roughly 12% of men in the same age range[59].

Migraines are typically treated with triptans and isometheptene, together comprising 99% of antimigraine prescriptions [59]. 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[269]. Other medications, including ergots also have some evidentiary basis [270], but comprise <1% of antimigraine prescriptions [59].

Dietary and lifestyle factors may play a role in migraine prevention, which has been covered by a superb 2018 review by Rehman et al. [271]. Table 9 below summarizes the interventions which can be used for the treatment of bowel pain.

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

Intervention	Effect on Migraine
Vitamin D	Symptom improvement [101,272]
Multivitamin (2 mg of folic acid, 25 mg vitamin B_6, and 400 µg of vitamin B_{12})	Improvement [273]
Magnesium	Oral magnesium alleviates the frequency and intensity of migraine[274]
Vitamin B2	Improvement [275]
Folic acid with pyridoxine	Decrease in headache severity [276]
Probiotic	No effect [277]
Feverfew	Low quality evidence for preventative effect [278]
Butterbur	Preventative effect [279] but possible health issues [280]
Meditation	Improved pain tolerance [281]
Yoga	Reduced headache frequency [282]
Tai Chi	Decreased stress in Chinese women with migraines [283]
Melatonin	Low quality evidence for improvement [284]
Ginger	Better treatment efficacy when used adjunctively with ketoprofen [285] Similar efficacy to drug sumatriptan [286]
Omega 3	Reduction in duration [287]
Ginkgolide B	Reduction in migraine with aura frequency and duration [288]

Limited evidence exists currently to make solid recommendations [289]. Riboflavin, magnesium and Coenzyme Q10 may reduce the pain severity from migraines [100]. Vitamin D markedly reduces

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the frequency of migraine attacks per month, but has non-significant impact on migraine severity[272].

Among obese adolescents, a weight loss program focusing on dietary education and exercise significantly lowered headache frequency and intensity [290]. The herb Tanacetum may decrease migraine pain, especially when combined with acupuncture [291].

Together, integrative techniques may reduce the incidence and severity of migraines and headaches, which often cause people to turn to opioids.

Common Elements

Some interventions are suitable for pain emerging form multiple sources. These are summarized in Table 10 below.

Table 10. For those interventions acting on pain emerging form 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	+[292]	+[293]	+ [294]	+ (animal model) [295]	+ [296,297]
Rheumatoid Arthritis	+[142]	+ [298]	+[299,300] n.s. [301]	+ (animal model) [302]	+ [303–305]
Injuries or Injury risk	+ (running injury risk)[306]	Unknown	+ (case series) [307]	+ [308,309]	+ [310]
Low Back Pain	+[311]	+ [195]	+[312–314]	n.s. [129]	+ [206,315]
Post-surgical pain	n.s. [316]	+ (animal model) [317]	+ [318]	+ [125]	+ [319,320]
Cancer pain or chemotherapy pain	n.s.*[321,322]	n.s.† [323]	+ [324,325] n.s. [326]	+ [327]	+ [328,329]
Fibromyalgia	n.s. [330]	+ [331,332]	+ [333–335] n.s. [336,337]	+ [338]	+ [339–341]
Neuropathic pain	+ (case series) [342]	+ [343]	+ [344,345]	+ [346,347]	Partial response [348]
Migraine	+ (reduction in migraine duration) [287]	+ [349]	+ [350,351]	+ [352]	+ [353,354]

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Conclusion

Chronic pain is currently a major 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 individual 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 to be built upon by developing rigorous trials of interventions, and then bringing these out to the public.

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