



## 40 Years of Progress and Future Directions in Chronic Pain Management and Patient Safety

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Although pain has been a primary reason to seek medical treatment for centuries,<sup>1</sup> pain management has only been a medically recognized multidisciplinary subspecialty since 1992.<sup>2</sup> Since then, pain specialists have expanded, refined, and innovated their practices to meet the growing needs of their patient populations, with considerable improvements in patient safety.

### GLOBAL PREVALENCE OF PAIN

Pain is the leading cause of disability, and its prevalence is increasing worldwide.<sup>3</sup> Low back pain, the number two cause of Disability-Adjusted Life Years worldwide, affects over 619 million people, approximately 10% of the 2020 world's population.<sup>4,5</sup> The prevalence of unspecified persistent pain in low to middle-income countries is estimated to be 34%.<sup>6</sup> In 2022, the World Health Survey was used to model the prevalence of pain across over 52 countries, identifying an average prevalence of 27.5%, ranging from 9.9% in China to 50.3% in Morocco.<sup>7</sup>

The global prevalence of pain is influenced by several factors. At the individual level, female gender, older age, and rural versus urban living environments are associated with higher pain prevalence.<sup>7</sup> At the country level, factors associated with increased pain prevalence include population density, life expectancy, gender inequality, and income inequality.<sup>7</sup> The reported prevalence of pain is also intimately related to the frequency of surveillance, and surveillance for pain is often ignored in lower income countries. According to the 2021 Global Burden of Disease study, the most dramatic growth in prevalence of low back pain is expected in Asia and Africa, where many of these country-level inequalities may be more pronounced.<sup>5</sup>

### SOCIOECONOMIC IMPACT OF PAIN

Aside from disability, chronic pain also exacts a major socioeconomic toll on individuals and societies. The National Health Service in the UK spends nearly £5 billion annually on general practitioner evaluations of low back pain.<sup>5</sup> In the USA, the health care expenditures for low back and neck pain in 2016 was an astonishing \$134 billion.<sup>5</sup> In addition to direct health expenditure, there are the additional socioeconomic costs of absenteeism, presenteeism, and productivity losses, which far exceed direct costs. The effect of low back pain on the ability to work is even more profound in low to middle-income countries, where known risk factors for chronic pain may be accentuated.



### MEDICAL MANAGEMENT OF CHRONIC PAIN

The medical management of chronic pain has long been fraught with complexity and has historically centered on pharmacologic solutions—particularly opioids. In the late 20th century, pain was reframed as the “fifth vital sign,” prompting a dramatic increase in opioid prescribing, often with insufficient evidence and an underestimation of the risks of dependence, tolerance, and hyperalgesia.<sup>8,9</sup> A focus on symptom management and ignoring the individuality of pain perception gave rise to a widespread overreliance on chronic opioid therapy. The fallout of this approach has been well-documented as the global opioid crisis.<sup>10</sup> Even without opioids, chronic pain management often relies on “synergistic” polypharmacy despite side effects like somnolence, mood and memory impairment, fatigue, and organ dysfunction. These treatments are associated with adverse reactions, cognitive decline, falls, and hospitalizations, particularly in elderly and complex patients.<sup>11</sup>

### ADVANCEMENTS IN THE UNDERSTANDING OF PAIN

Research in the mechanisms of chronic pain has increased substantially in the last 40 years, leading to new understandings in pain signaling. Early research identified neurologic pathways and differentiated the types of nerve fibers involved in pain transmission.<sup>2</sup> Further studies elucidated more mechanisms for pain such as the descending inhibitory system, the endogenous opioid system, and the contribution of the autonomic nervous system. Newer

research, especially utilizing functional MRI and other biomarkers, further explores the brain's dual role in the processing of chronic pain. Specifically this has identified not only the sensory-discriminative (e.g., location and intensity) components, but also the under-appreciated yet equally important affective-motivational and cognitive-evaluative (e.g., emotional and attentional) components.<sup>12</sup> Recently, two new classes of medications have been developed: selective NAV1.8 receptor inhibitors intended for acute pain management and CGRP (calcitonin gene-related peptide) inhibitors intended for migraine treatment.<sup>13</sup>

John Bonica, a pioneering anesthesiologist and former wrestler who suffered from chronic pain himself, seemingly anticipated these findings when he started the first multidisciplinary pain program in 1961.<sup>2</sup> Multidisciplinary pain clinics address the medical needs of patients using a biopsychosocial model. The biopsychosocial model of pain acknowledges the multidimensionality of pain as unique physical, psychological, and social factors shape it.<sup>14</sup> The limitations of pharmacotherapy and interventions targeting pain as a symptom are now the catalyst for a shift towards a more integrated, patient-centric care framework. Such an approach incorporates psychological support and lifestyle interventions into the treatment algorithm. Patients supported with lifestyle changes often report reduced pain alongside mood, energy, and quality of life improvements.<sup>15-17</sup> These approaches seek to address some of the underlying causes of

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inflammation, metabolic dysfunction, and stress and are especially valuable for those seeking noninvasive, self-directed care.<sup>18</sup> Multidisciplinary pain clinics that address the biopsychosocial model reduce emergency room visits, medication costs, and overall health care utilization. Further, patients of multidisciplinary clinics report less pain, have higher pain-related health literacy, and experience less pain-related limitations on their activities.<sup>19</sup>

### ADVANCEMENTS IN INTERVENTIONAL PAIN MEDICINE

Interventional management of pain has also seen major advancements in patient safety. Perhaps the most important safety development has been the use of image guidance which allows for precision needle placement, surveillance of injectate spread, and detection of vascular uptake. Well into the early 2000s, high-impact general medical and specialty journals published clinical studies and case reports evaluating the effectiveness of commonly performed procedures such as epidural steroid injections (ESI), and high-risk procedures such as stellate ganglion block and celiac plexus neurolysis, done blindly without image guidance, sometimes with catastrophic consequences.<sup>20-22</sup> The use of imaging, which now includes real-time injection under fluoroscopy and ultrasound guidance, and in some cases computed tomography, has significantly improved outcomes and reduced complications.

### SAFETY RESEARCH IN INTERVENTIONAL PAIN

A second advancement in safety has paradoxically been payor requirements for clinical

studies to support various procedures, including high-risk ones, that previously were being widely performed based on anecdotal evidence and often biased by conflicts of interest. Previously commonly performed procedures that have been debunked by high-quality studies are intradiscal procedures (e.g., intradiscal electrothermal therapy and methylene blue injection). These can result in a subsequent increased risk of disc herniation, accelerated degeneration, and clinical deterioration. A second area in which payor pushback has resulted in improved safety is the use of sedation for routine procedures such as ESI, facet blocks, and sacroiliac joint injections. According to some studies, sedation was used through the 2010s in around half of all lumbar ESI. When used indiscriminately, deep sedation not only dramatically increases the cost of procedures, but has also been shown to increase the risk of complications and false-positive diagnostic blocks, leading to unnecessary procedures such as radiofrequency ablation and celiac plexus neurolysis, and overall poorer treatment outcomes.<sup>23,24</sup>

Identifying the prevalence and risk factors for rare but catastrophic complications is often impossible based on clinical studies, but relative risks can be ascertained by large database reviews, such as what U.S. Food and Drug Administration (FDA) investigators did for epidural steroid injections. The evidence for epidural depo-steroid injections is stronger than for injections performed with non-depo-steroids, so determining whether depo-steroids are associated with greater risks during lumbar transforaminal injections for sciatica is important for proper evaluation of risk vs benefit.<sup>6</sup> In the aforementioned FDA study, the authors could not find a difference in complication rates between particulate (depo) and nonparticulate steroids for transforaminal injections in over 1 million Medicare patients.<sup>25</sup>

### LIFESTYLE MEDICINE

Prescriptive lifestyle approaches are invaluable in pain management for sustainable analgesia, decreased pain perception, and functional improvement, which may be more sustainable and safer than pharmacotherapy.<sup>26,27</sup> Mindfulness-based stress reduction, breathwork, and cognitive behavioral therapy help with coping, distraction, anxiety mitigation, and stress management, increasing agency and resilience while decreasing pain perception.<sup>27</sup> Quality sleep is also essential to pain modulation as circadian disruption and sleep dysregulation correlate with heightened pain sensitivity, anxiety, and reduced pain tolerance. Several integrative practices such as acupuncture, yoga, virtual reality, massage, and tai chi offer excellent low-risk alternatives. Physical activity decreases neu-

roinflammation and modulates pain signaling while also enhancing resilience, strength, circulation, and mobility.<sup>28</sup> In addition, it can also improve sleep and mood, thereby creating a virtuous cycle. Anti-inflammatory diets help modulate pain and improve mitochondrial and glial function.<sup>29</sup> Diets rich in omega-3s, antioxidants, and sirtuins reduce systemic inflammation while low-FODMAP (Fermentable Oligo-, Di-, Mono-saccharides And Polyols) diets modulate serotonin. Addressing chronic inflammation, supporting gut health, and promoting neuroprotection with such diets may additionally impact disease progression.<sup>30,31</sup> Improved sleep with behavioral techniques, relaxation, regular sleep-wake cycles, light exposure, melatonin, and cognitive behavioral therapy for insomnia—are linked to reduced pain and improved health biomarkers.<sup>32</sup>

### THE FUTURE: POLICY CHANGES AND GLOBAL HEALTH

Addressing pain on a global scale requires appropriate public health and health policy measures. This is especially important given that many low- and middle-income country governments do not prioritize pain management services, instead focusing on the treatment of communicable diseases. Raising awareness of the individual-level and country-level impact of untreated chronic pain is a logical starting point. A comprehensive health policy and public health approach will likely involve a combination of awareness of the impact of chronic pain, and education on how to prevent and treat chronic pain. Advocating for access to appropriate, cost-effective treatment options within a country's resource limitations is also key.

An example of where this approach has been successfully implemented is in Southeast Asia through the Association of Southeast Asian Pain Societies (ASEAPS). Over a 20-year period, the ASEAPS has systematically and collaboratively worked to improve awareness and access to multidisciplinary pain care. Through a coordinated approach that involves multilevel education and training of clinicians, the ASEAPS, in conjunction with the International Association for the Study of PAIN (IASP), has successfully increased access to multidisciplinary pain centers in the region.<sup>33</sup>

Ultimately, in a world where the prevalence and impact of chronic pain continues to rise, it is in our best interest to intentionally develop public health policy and education campaigns designed to both raise awareness and encourage appropriate action to increase access to effective pain management care.

### THE FUTURE: INTERVENTIONAL PAIN

As medicine in general shifts to a more personalized treatment paradigm, this will inevitably

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bly improve both the risk to benefit and the cost to effectiveness ratios, paving the way for more efficient resource allocation and better outcomes. For example, ESI and riskier, more costly procedures such as spinal cord stimulation where the data on effectiveness shows tremendous variability, are purported to provide benefit to approximately half the patients who receive the treatment. Yet with phenotyping, or identifying unique characteristics associated with treatment outcome, we will someday be able to accurately predict which patients will improve and which patients will not. For some comorbidities such as obesity, diabetes, and central sensitization, studies evaluating multiple procedures have even shown complication rates to be higher.

## THE FUTURE: PERSONALIZED PAIN MEDICINE

The implementation of lifestyle models of care aligns with broader health care goals of harm reduction and minimizing health care disparities harm by treating patients as partners rather than passive recipients of prescriptions and invasive interventions. It is safe, scalable, and easily adaptable across communities and cultures. The shift to integrate lifestyle medicine supports improved adherence, reduced hospitalizations, and improved outcomes across domains beyond pain, including metabolic, cardiovascular, and mental health.

Emerging digital tools, remote monitoring, telemedicine, and artificial intelligence-driven risk stratification may improve safety and personalize care.<sup>34</sup> Harnessing these technologies may be of great value in identifying complications, nonadherence, or noncompliance without delay. They may also aid in improving self-efficacy and engagement. Such approaches to care may be transformative within populations with barriers to accessing specialty care or navigating fragmented health care systems. For individuals who may experience adverse outcomes from overmedicalization, or risks associated with polypharmacy and invasive interventions, lifestyle strategies are safe, sustainable, and offer a culturally adaptable path to acceptable health outcomes.

A paradigm shift will require considering such an approach not as a soft alternative to conventional care, but as a necessary evolution. As health care systems worldwide strive to become equitable, safer, and person-centered, lifestyle-based and root-cause approaches must be at the forefront—not only for their clinical efficacy—but also for their capacity to uplift, engage, and sustain the well-being of populations.

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