

Perspective

Reframing The Role of Neuromodulation Therapy in the Chronic Pain Treatment Paradigm

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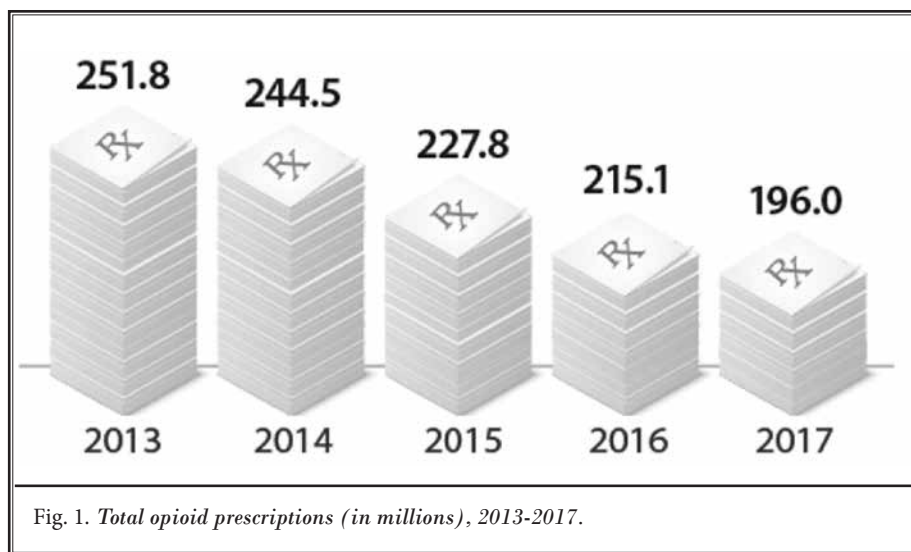
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The most important advances in medical science are derived from facts and real-world evidence (1). However, the importance of proper evidence synthesis and preparation of clinical practice guidelines continues to be subjected to extensive debate with discordant conclusions, despite release of the document by the Institute of Medicine (now National Academy of Medicine) in 2011 (2). This has been considered as an important step towards better evidence synthesis and clearer guidelines. Evidence synthesis and clinical practice guidelines are an important part of medical practice, but scarce funding for updates, competing organizations issuing their own, sometimes conflicting, guidelines, and the risk for bias and conflicts of interest have raised challenges (3). Critical review of statistics surrounding the current opioid epidemic reveal that the most compelling statistic in 2017 was health care providers across the U.S. wrote about 196 million prescriptions for opioid pain medication as shown in Fig. 1 (4). Consequently, the opioid epidemic has been called “the most consequential preventable public health problem in the United States.” Despite a multitude of regulations and declining use of opioids, opioid-related deaths increased 3.7% from 2016 to 2017 in the face of an explosive increase of deaths due to synthetic opioids of 46%, cocaine of 37%, and methamphetamine of 40% (Fig. 2). The major underlying issues in heroin epidemic is based on opioids as gateway drugs (4-7). Multiple regulations focus



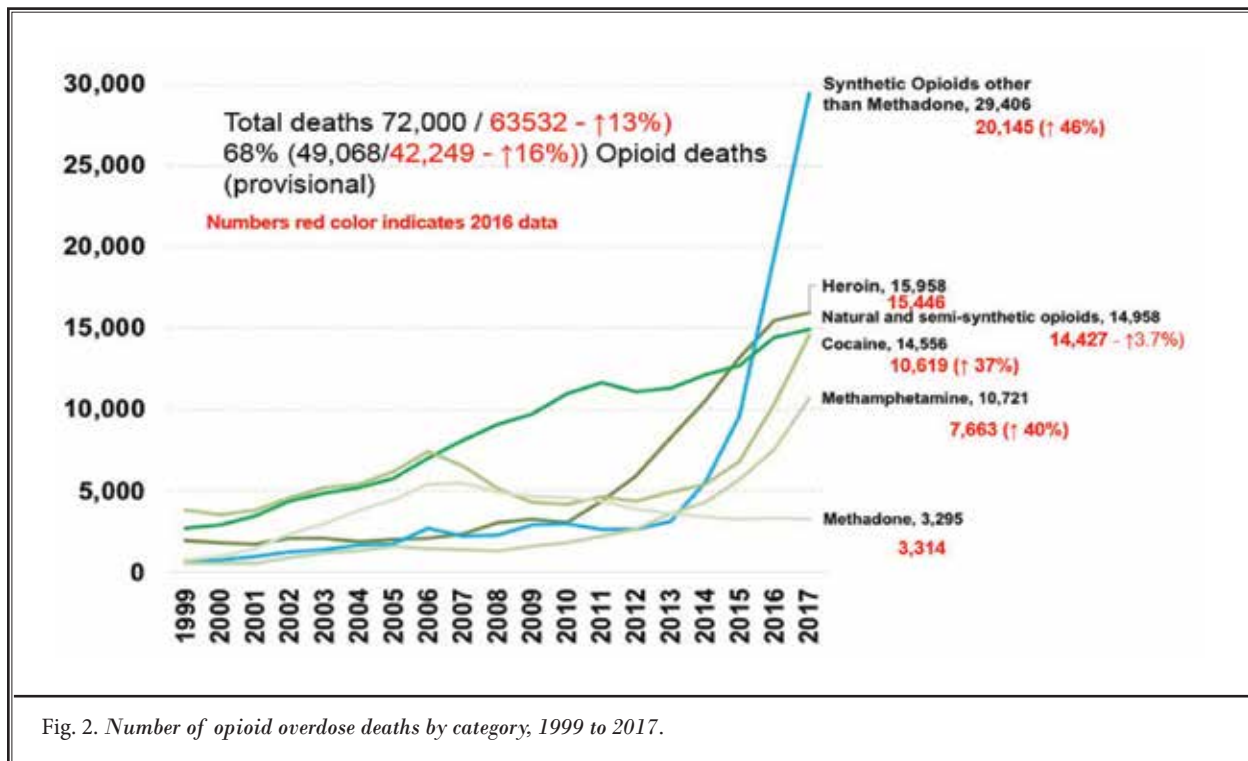
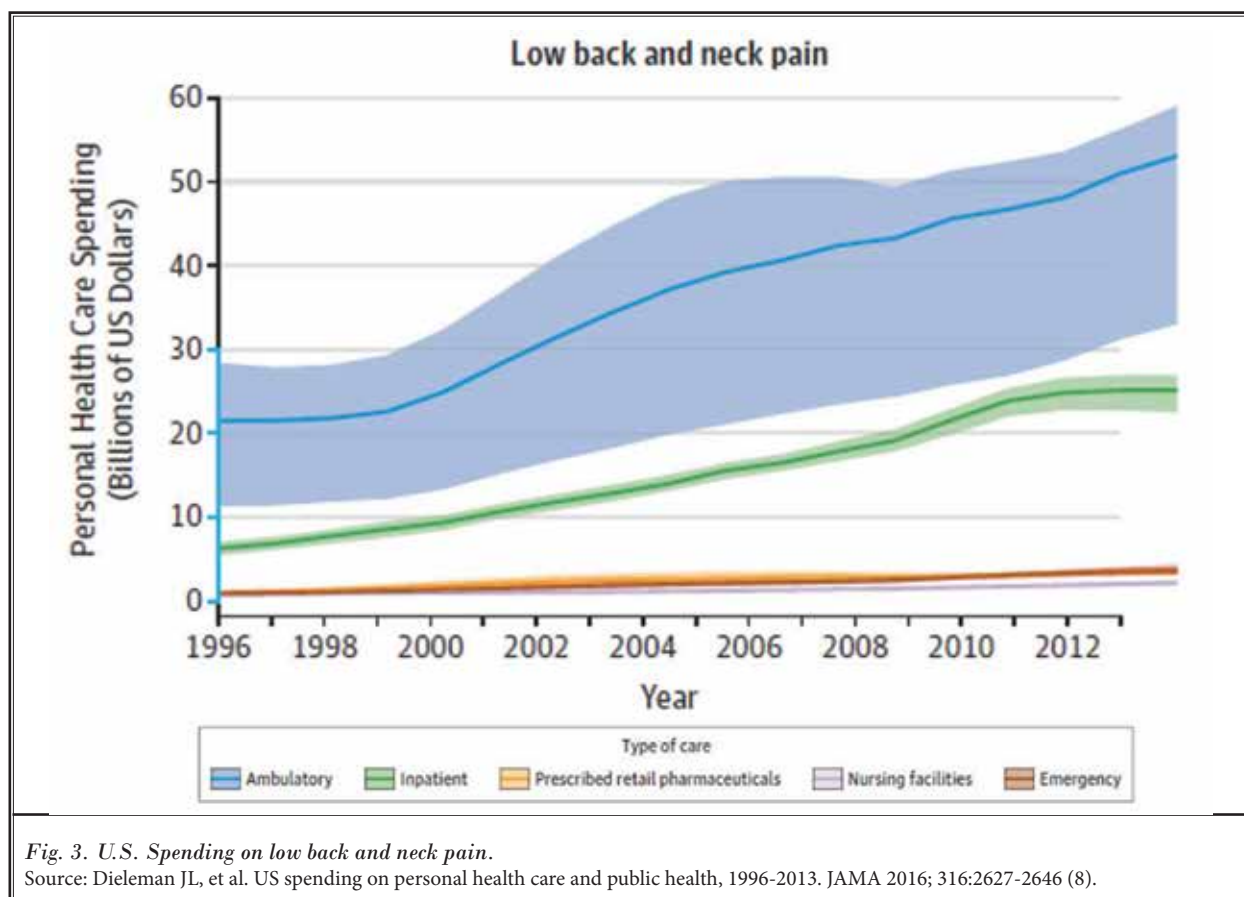


Fig. 2. Number of opioid overdose deaths by category, 1999 to 2017.

on controlling the opioid epidemic by reducing opioid production and discouraging opioids as a therapeutic option. Reframing of the prevention strategies of the opioid crisis continues to lag behind the escalating epidemic (5-7). At the same time, the impact of chronic pain, and specifically of spinal pain, continues to escalate, by some accounts even higher than those for cancer, heart disease, and diabetes. Combined with low back pain and neck pain, spinal pain ranks among the top 5 conditions of disability with annual expenditures of \$87.6 billion in 2013 (8,9). These glaring statistics are not simply related to opioid prescriptions and health care expenditures, but to the presumed lack of effective treatment alternatives, despite advances in pharmacology and surgical interventions (Fig. 3) (6-10).

When Norman Shealy placed the first spinal cord lead 40 years ago, he would not have imagined the growth in technology and innovation the field of neuromodulation has seen over the last half-century (11-19). Inspired by the seminal gate-control theory of pain, which was proposed by Melzack and Wall (20), the conventional paradigm of spinal cord stimulation (SCS) involves tonic 40-60 Hz electrical stimulation that activates dorsal columns in the spinal cord to elicit

paresthesia covering the patient's painful body regions (19,21). This paresthesia-based SCS has proven to be an effective treatment modality for 40-50% of patients with refractory pain conditions, including complex regional pain syndrome (CRPS) and failed back surgery syndrome (FBSS) (21,22). The last decade has seen rapid innovation in the development of new neuromodulation therapies, largely based on the rapid pace of neuroscience discovery (18,19). These developments include high-frequency stimulation, burst stimulation, dorsal root ganglion stimulation, as well as a plethora of more sophisticated outcomes data. The body of evidence for SCS as an effective and long-term treatment for chronic pain is robust and growing. However, awareness of the therapy has been mostly limited to spine surgeons (orthopedic and neurosurgery) and interventional pain physicians (18,22-30). Given the staggering implications of chronic pain and associated disability with numerous ongoing treatment options, including surgical interventions, other interventions, and opioid prescriptions (4-8,10,24-32), it is clear that the medical community, ranging from primary care physicians to surgical specialists, who treat chronic pain patients on a daily basis, are unaware of the advances

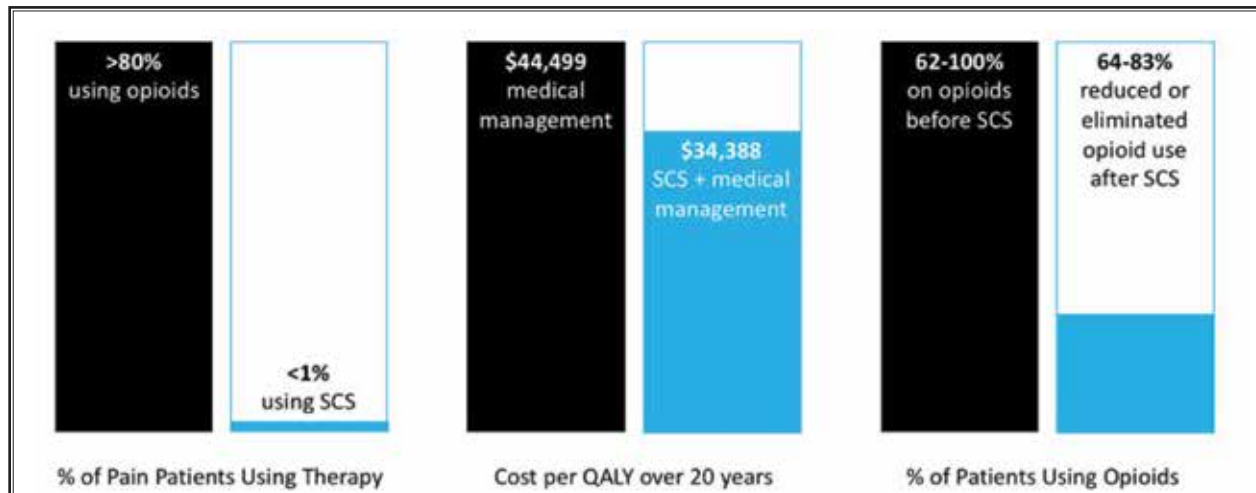


of neuromodulation and its potential adoption into pain treatment algorithms. Today's neuromodulation systems are no longer an extension of anecdotal data driven by industry-funded science, but evidence-based treatment for chronic pain patients that demonstrate a significant improvement in efficacy compared to alternative treatment modalities (18,19,21-23,28). Referring physicians of all disciplines should and must be encouraged to examine the evidence and provide appropriate referrals for comprehensive management of disabling chronic pain, to interventional pain physicians in the community offering evidence-based approaches, including neuromodulation. Consequently, lack of awareness can no longer constitute failure to provide a potential treatment alternative with demonstrated efficacy and limited side effects.

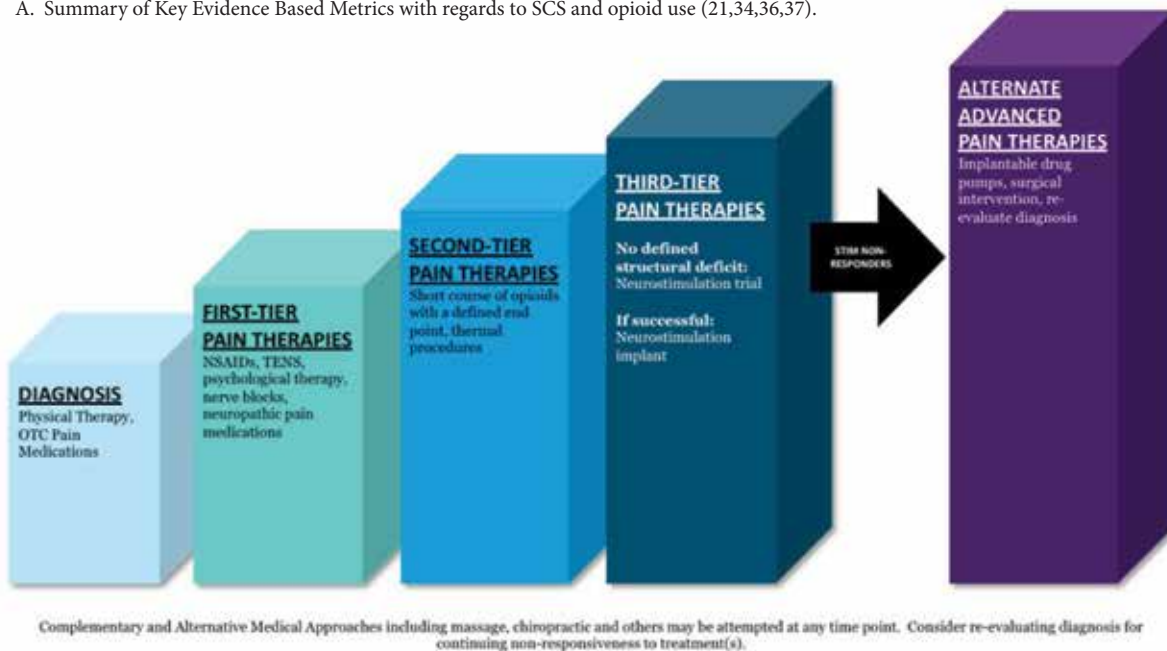
EVIDENCE TO VALUE-BASED

SCS has been shown to retain its efficacy in multi-year follow-up studies (18-23,32), whereas a review of the evidence of opioid therapy for chronic pain has

demonstrated limited data of long-term effectiveness of opioids beyond 3 months (5-7). Historically, patients living with chronic pain have had to undergo significant trials of opioid medications, other pharmacological therapies, and other procedural interventions in order to 'qualify' for neuromodulation therapy, which was positioned as a last-line therapy. A real-world analysis of claims data demonstrated that patients that were given high (average 73 mg/day) and increasing dosages of opioids before receiving SCS (33) ultimately increased the patient's risk for system explant by 57%. High dosage opioid use was also associated with other poor outcomes, such as longer postoperative stays and damped improvement of pain scores (34). Delaying the use of SCS by just one year was shown to increase the risk for higher healthcare expenditures by a staggering 33% (35). New evidence is emerging that shows SCS can help interrupt dependence on opioid medications. For example, in a trial of BURST SCS, 83% of patients had reduced or eliminated opioid use after receiving SCS, and similarly, 64-70% of patients had reduced or



A. Summary of Key Evidence Based Metrics with regards to SCS and opioid use (21,34,36,37).



B. Proposed modification of the chronic pain treatment continuum.

Fig. 4. Support for evidence to value-based platform.

eliminated opioid use in other single-center, randomized control, and real-world studies of SCS (36,37). Figure 4A summarizes these key points.

REFRAMING THE CURRENT TREATMENT PARADIGM FOR CHRONIC PAIN

Reframing of the current treatment paradigm for chronic pain essentially requires comprehensive assess-

ment of chronic pain patients and more rapid progression through various modalities with avoidance or extremely limited use of opioid therapy. Interestingly, Shealy described stimulation in favor of ablation in 1968 (13) and specialization and development of Centers of Excellence in 1974 (15). In the modern era of exploding health care costs, adverse consequence of numerous modalities of treatments, and continued expansion of

disability development of comprehensive chronic pain management therapy with earlier application of spinal cord stimulation is an important approach.

Figure 4B is a proposed treatment algorithm to consider how SCS therapy could fit into the chronic pain treatment paradigm. One of the key aspects of stimulation therapy is that, unlike surgery or lesioning, it is reversible (13). The implant procedure requires a trial period during which a temporary stimulation system is used to test for therapeutic benefit before proceeding to device implant. The use of the trial period and its reversible nature supports stimulation therapy to be in an earlier tier prior to consideration of other advanced pain therapies, such as surgery, intrathecal therapy, or chronic opioids for non-cancer pain that are not easily reversible. Kumar's data is compelling showing 85% success rate if implanted less than 2 years of the pain diagnosis (38). Good response to trial stimulation more recently has anecdotally correlated consistently with a response to therapy post implantation above 80%.

THE FUTURE OF SCS THERAPY

Chronic pain is a complex disease process, often leading to a biopsychosocial disorder if not treated properly. As CMS administrator, Seema Verma (39,40) noted, physicians have received years of education, training, and hard work to develop a high level of expertise, which is not utilized appropriately, and instead, they are being forced to spend far too much of their time on burdensome and often mindless administrative tasks. The systems have taken the most brilliant students and put them to work clicking through screens and copying and pasting, with 42% of physicians reporting burnout. Thus, as physicians we must reflect not only on the opioid epidemic, but also the epidemic of chronic pain and disability. We must utilize our knowledge and advances, driving the optimal care of patients and removing them from the present state of a disability-driven health care system. Thus, neuromodulation offers an alternative by professionals trained in the management of chronic pain in a shifting paradigm of value-based health care with both increased emphasis on patient and physician quality of care.

This is not to promote neuromodulation without further research. It is crucial to perform appropriate clinical trials and establish real world data to improve clinical guidelines and ultimately clinical practice. We should remember the quote by Sir Arthur Conan Doyle which states, "Education never ends. It is a series of lessons, with the greatest for the last", complemented by Michelangelo's quote at age 87 of "I'm still learning."

It is time to educate physicians and patients on another very viable tool in the pain therapy arsenal – neuromodulation. Earlier consideration in appropriate patients by every medical practitioner treating pain can help replace opioid therapy with a presently reversible, safe, and effective therapy.

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