

## EDITORIALS

---

# Rethinking Algorithms of Pain Care: The Use of the S.A.F.E. Principles

### Introduction

In 1996, Krames, trying to make sense out of therapeutic choice for pain management of chronic noncancer-related pain problems wrote that “because there are multiple choices, both interventional and noninterventional for the management of pain, the treating physician should choose one therapy over another in a rational manner . . .” [1] Because, at the time there was little information to mine for decision-making, the only variables accessible to the treating physician for choosing one therapy over another were levels of invasiveness and “up-front” costs of the therapy. Krames suggested an algorithm of choosing that was based on the time-honored medical principle, the KISS principle, or “Keep It Sweet and Simple.” This algorithm based on the KISS principle listed least invasive and less “up-front” costly therapies first and more invasive and more costly therapies, later in the algorithm. He also suggested that some therapies could be used in series, some in parallel, abandoning those that do not work and trying more invasive therapies and more costly therapies until the algorithm (choices) was exhausted. Based on this algorithm, implantable technologies for pain, stimulation therapies, and implantable drug delivery systems (IDDS) were relegated to last resort therapy.

While this approach was appropriate for the time, today, a review of the literature allows us to make more rational choices between pain therapies based on variables other than invasiveness and up-front costs. Today, it may not be in the best interest of a patient, or even the third party payer, to wait until all less costly and less invasive, but not effective, treatment options have failed before initiating more invasive therapies including nerve-blocking procedures, epidural steroid injections, facet injections/neurolysis, or therapies of neuromodulation, such as spinal cord stimulation (SCS), peripheral nerve stimulation (PNS), peripheral subcutaneous field stimulation (PSFS), or intrathecal therapies via IDDS. If a given procedure or

technology is more effective and more cost-effective over time, it may be best to offer that therapy sooner rather than later. While many more invasive therapies and certainly neuromodulation therapies may *initially* be more expensive than more conventional therapies, such as physical therapy and medication management, they may be more cost-effective over time [2,3], reaching a point in time where the more invasive therapy becomes less costly, a point that is called *cost neutrality*. It is their superior effectiveness and long-term cost-effectiveness that challenges the notion that invasive procedures or neuromodulation therapies should be at the end of a treatment algorithm. For example, North et al. [4] showed, in a randomized controlled study, that those patients with persistent neuropathic leg pain treated with SCS after appropriate neural decompression did better when comparing efficacy outcome and cost than those treated with repeat surgery.

Mining the literature for information regarding therapies for pain management today, there is more information than just levels of invasiveness, up-front costs, and efficacy. There is information on appropriateness of the therapy for any one individual, information on safety of the therapy, information on cost-effectiveness of the therapy, and information on cost neutrality of the intended intervention. With this information, physicians and, to a certain extent, entities that pay for the procedure can and should make more rational decisions regarding the use of interventions for patients with chronic pain. We propose a set of principles for algorithmic evaluation of pain care therapies, the S.A.F.E. principles: Safety, Appropriateness, Fiscal neutrality, and Efficacy.

### Principle of Safety

Persistent chronic pain is rarely life-threatening and treatment algorithms should be held to a higher standard of safety than treatment algorithms intended to treat life-threatening illness

such as advanced cardiac life support algorithms. All invasive procedures including neuromodulation technologies are inherently associated with surgical risks such as infection, bleeding, and/or injury to neural tissues. As such, the positioning of invasive therapies including neuromodulation therapies (SCS, PNS, PSFS, etc.) within an algorithm to treat persistent chronic pain has traditionally come after trials of less invasive treatments such as medication management [1]. Medication use may certainly be less invasive, but their use may be more harmful over time than more invasive therapies. For example, the chronic use of nonsteroidal anti-inflammatory agents (NSAIDs), what most would consider a conservative analgesic therapy, has increased risk of injury over time. Chronic use of NSAIDs for pain management, however, is associated with a 17–31% incidence of gastric ulcer formation, leading to 16,500 deaths and more than 100,000 hospitalizations every year in the estimated 20 million patients taking chronic NSAIDs in the USA [5–8]. By comparison, the greatest biological risks of SCS for chronic pain occur during the operative and postoperative periods with infection and seroma being the most common complications. In a 10-year retrospective study of 160 patients treated with SCS, Kumar et al. reported a total of 7.5% biological adverse events with 4.4% incidence of infection (three requiring i.v. antibiotics) and a 3.1% incidence of seromas (one requiring surgical evacuation), and no neural injury or death [9]. While this sample size is clearly far less than those samples evaluating chronic NSAID use, these results nonetheless, in our estimation, support the hypothesis that the risk of injury from chronic usage of NSAIDs (less invasive, more conservative) is greater than the risk of injury caused by long term treatment with SCS (more invasive).

### Principle of Appropriateness

Certainly, when determining whether a given treatment is appropriate for inclusion into a medical algorithm to treat persistent pain, it is of equal importance to secure the diagnosis as well as confirm the absence of any pertinent medical or psychosocial contraindications. Everyone would agree that patients with peptic ulcer disease or those with renal failure should not be treated with NSAIDs or that chronic opioid therapies should be avoided if possible in patients with underlying drug addictions. Likewise, systemic infections and

coagulopathies are medical contraindications and premonitory psychiatric illnesses such as schizophrenia or conversion disorders are psychiatric barriers to performing elective invasive procedures. Disregarding these contraindications increases the risk of injury to patients and may result in additional cost to treat these added complications. Because the use of invasive therapies including implantable neuromodulation devices is costly to the patient and those who pay for the therapy, it is critical that appropriate measures be taken to insure that only suitable patients are so treated.

### Principle of Fiscal Neutrality

Health care costs currently account for 16% of the US gross domestic product, an increase from 9.4% in 1980, and are expected to rise to 20% by 2015[10,11]. While the high cost of medical technology use is only one of many reasons for this increase, many physicians and policymakers point to unnecessary use of medical technology as a major contributor to the rising cost of health care [12,13]. With shrinking resources and increased demand, health administrators struggle to allocate appropriate resources while maintaining fiscal responsibility. As a result, third party payors and nonpain management physicians are reluctant to authorize or refer patients for invasive therapies including neuromodulation technology as part of a treatment algorithm for persistent pain. Thus, appropriate positioning of neuromodulation technology within a treatment algorithm for persistent pain must account for the financial implications of this treatment, with fiscal neutrality, not up-front costs, being the financial goal for implementation. In this context, fiscal neutrality implies that the cost of implementing a new therapy does not result in greater financial expenditure than a current or comparator therapy over a given time period.

Some examples illustrate the “cost neutrality” principle. When compared with conventional medical management strategies for chronic pain, some authors found that implanted intrathecal opioid delivery was cost-neutral at 22–28 months after implant, and generated a cost-savings thereafter [14–17]. Fiscal neutrality may even be achieved on day one when compared to other surgeries as observed by North et al. in their study of SCS vs conventional repeat spine surgery (reoperation) for treatment of failed back surgery syndrome (FBSS) and Andrell et al.’s

study of SCS vs coronary artery bypass surgery for intractable angina [4,18]. In fact, implementing SCS was actually a cost savings when compared to repeat spine surgery or cardiovascular surgery. Taylor and Taylor estimated that when compared to conventional medication management, SCS was more effective and less costly when treating FBSS over the lifetime of a patient [19]. Shorter time to fiscal neutrality was observed for treatment of complex regional pain syndrome. SCS was found to be fiscally neutral in as little as two and a half years after implantation when compared to standard focused physical therapy treatment alone [20]. In a review of the literature, Taylor et al. reported that the time to fiscal neutrality when using SCS was 1–3 years in a variety of pain conditions [21].

### Principle of Effectiveness

Certainly, doing the right thing is what clinicians hope to achieve for their patients; guiding their actions are training, experience, colleagues, and the medical literature. Alone, the medical literature is insufficient to guide clinical judgment; yet, it is certainly essential when developing medical treatment algorithms of care.

Many treatment algorithms for the medication management of persistent pain conditions are developed after compiling data from a number of randomized double-blind, placebo-controlled clinical trials [22–24]. Demonstration of efficacy alone, utilizing robust scientific methods as well as designed randomized controlled trials, is not sufficient to mandate implementation of a given treatment into a clinical algorithm. Indeed, third party payers and government agencies may require a broader base of evidence to support implementation of a given treatment. Clearly, this was the case when former Secretary of Health and Human Services Patricia Roberts Harris declared in 1980 that new health technologies must be evaluated not only on the basis of their medical efficacy but also on their “social consequences” before any consideration could be given to federal reimbursement for the new device or procedure [25,26]. As such, implementation of a given therapy for pain should be judged by more than just a change in pain scores.

In addition to clearly establishing the appropriate outcome measures to be used when comparing various therapies, it is also critical to determine the appropriate level of evidence for comparing invasive therapies with other, less invasive treatment

options. Typically, studies aimed at comparing different medication therapies are performed by utilizing a large-scale, placebo-controlled, double-blind design. However, in clinical trials of neuromodulation, placebo-controlled, double-blind studies of implanted technologies are nearly, but not totally, impossible to conduct for both technical and ethical reasons [27]. Certainly, the risks of surgical intervention are too great to justify sham surgeries for clinical design and this position is supported by the 2000 revision of Declaration of Helsinki which reinforces the prohibition against offering placebo instead of effective therapy [28]. Blinding can also be difficult in clinical trials of neurostimulator devices as many of these devices can and are sensed by the patient when turned on and likewise, sensed when turned off [29].

In spite of these caveats, there is still ample evidence to demonstrate effectiveness of neuromodulation technology for the management of persistent pain, and implementation of this evidence certainly meets the definition of evidence-based medicine [30–32].

### Use of the S.A.F.E. Principles

Positioning of invasive therapies such as neuromodulation technology within a treatment algorithm of persistent pain has traditionally been relegated to the end of an exhaustive list of more conventional therapies. This “relegation to the end” of a continuum of care can sometimes lead to months if not years of poor pain control, prolonged medication toxicity, prolonged disability, excessive costs, countless interventional procedures, and increased risk of central nervous system reorganization before neuromodulation technology is offered [1]. We propose that the S.A.F.E. principles be the foundation on which to build algorithms for the treatment of persistent pain with invasive therapies such as neuromodulation (SCS, PNS) having an equal footing for evaluation as other less invasive therapies when developing these algorithms. By subjecting all therapies to a comprehensive evaluation using the S.A.F.E. principles, we believe that invasive therapies such as neuromodulation will be appropriately positioned in a continuum of care and not arbitrarily relegated to the end of the treatment continuum. Figure 1 is an example of how one would use the S.A.F.E. principles in a continuum of care for a patient with chronic nonmalignant pain from FBSS.

STEP ONE: less costly/efficacious therapies in parallel

- Exercise
- Over-the-counter analgesics/weak opioid therapies
- Injection therapies to reduce inflammation such as epidural lysis of adhesions, epidural depot of steroid, zygapophyseal joint denervation after positive joint blockade, etc.
- Physical restoration including movement therapies and postural training
- Cognitive and behavioural therapies to improve coping, reduce stress and improve self locus-of-control



PERSISTANT PAIN

Choosing three costly and efficacious therapies when all above have failed to provide long lasting relief of pain



- LONG TERM OPIOID MAINTENANCE with membrane stabilization
- ANOTHER RE-OPERATION OR
- SPINAL CORD STIMULATION (SCS) AND/OR PERIPHERAL NERVE FIELD STIMULATION (PNFS)



STEP 2: S.A.F.E. PRINCIPLES ANALYSIS<sup>4,14,15,16,17,18,19,20</sup>



- SCS and/or PNFS
- Long-term opioid and membrane stabilization maintenance or Intrathecal Analgesic Delivery Systems
- Another re-operation

**Figure 1** An example of how one would use the Safety, Appropriateness, Fiscal neutrality, and Efficacy (S.A.F.E.) principles for a patient with nonmalignant pain of failed back surgery syndrome, based on information mined from the literature. One would start with safe, efficacious and less costly therapies in parallel, in a judicious manner, abandoning those therapies that either do not work or only work for a limited amount of time. Evaluation of more up-front costly and more costly-over-time therapies would be evaluated using the S.A.F.E. principles.

### Acknowledgement

These authors acknowledge that they have not received editorial or financial support for their writing of this Editorial.

ELLIOT KRAMES, MD

*Director, Pacific Pain Treatment Centers,  
San Francisco, California*

LAWRENCE R. POREE, MD, MPH, PhD

*Director, Pain Clinic of Monterey Bay, Aptos,  
California, and Assistant Professor, Department of  
Anesthesia, University of California at  
San Francisco, San Francisco, California*

TIMOTHY DEER, MD

*President and CEO, The Center for Pain Relief, Inc.,  
Charleston, West Virginia, and Clinical Professor of  
Anesthesiology, West Virginia University, School of  
Medicine, Charleston, West Virginia*

ROBERT LEVY, MD, PhD

*Departments of Neurologic Surgery and Physiology,  
Feinberg School of Medicine, Northwestern  
University, Chicago, Illinois*

### References

- 1 Krames E. Interventional pain management appropriate when less invasive therapies fail to provide adequate analgesia. *Med Clin Am* 1999;83(3):787–808.
- 2 Krishna K, Malik S, Denny D. Treatment of chronic pain with SCS vs alternative therapies: Cost-effectiveness. *Analysis. Neurosurgery* 2002;51(1):106–16.
- 3 Kumar K, Taylor R, Jacques L, et al. SCS versus conventional medical management for neuropathic pain: A multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain* 2008;132(1–2):179–88.
- 4 North RB, Kidd D, Shipley J, Taylor R. SCS versus reoperation for failed back surgery syndrome: A cost effectiveness and cost utility analysis based on a randomized controlled trial. *Clinical studies. Neurosurgery* 2007;61(2):361–9.
- 5 Kozol RA. *Gastritis*. Boca Raton, FL: CRC Press; 1993.
- 6 Singh G. Recent considerations in nonsteroidal anti-inflammatory drug gastropathy. *Am J Med* 1998;105(1B):31–8S.
- 7 Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal anti-inflammatory drugs. *N Engl J Med* 1999;340(24):1888–99.
- 8 Fennerty MB. NSAID-related gastrointestinal injury: Evidence-based approach to a preventable complication. *Postgrad Med* 2001;110(3):87–9.
- 9 Kumar K, Wilson JR, Taylor RS, Gupta S. Complications of SCS, suggestions to improve outcome, and financial impact. *J Neurol* 2006;5(3):191–203.
- 10 Catlin A, Cowan C, Heffler S, et al. National health spending in 2005. *Health Aff* 2006;26(1):142–53.
- 11 Borger C, et al. Health spending projections through 2015: Changes on the Horizon. *Health Aff* 2006;25(2):W61–W73.
- 12 Iglehart JK. Opinion polls on health care. *N Engl J Med* 1984;310:1616–20.
- 13 Blendon RJ, Altman DE. Public attitudes about health-care costs. A lesson in national schizophrenia. *N Engl J Med* 1984;311:613–6.
- 14 Mueller-Schwefe G, Hassenbusch SJ, Reig E. Cost effectiveness of intrathecal therapy for pain neuro-modulation. *Neuromodulation* 1999;2(2):77–87.
- 15 Hassenbusch SJ, Paice JA, Patt RB, Bedder MD, Bell GK. Clinical realities and economic considerations: Economics of intrathecal therapy. *J Pain Symptom Manage* 14(3):S36–S48.
- 16 Lissovoy G, Brown RE, Halpern M, Hassenbusch SJ, Ross E. Cost-effectiveness of long-term intrath-



- ecal morphine therapy for pain associated with failed back surgery syndrome. *Clin Ther* 1997; 19(1):96–112.
- 17 Kumar K, Hunter G, Demeria DD. Treatment of chronic pain by using intrathecal drug therapy compared with conventional pain therapies: A cost-effectiveness analysis. *J Neurosurg* 2002;97:803–10.
  - 18 Andrell P, Ekre O, Eliasson T, et al. Cost-effectiveness of SCS versus coronary artery bypass grafting in patients with severe angina pectoris—long-term results from the ESBY study. *Cardiology* 2003;99:20–4.
  - 19 Taylor RJ, Taylor RS. SCS for failed back surgery syndrome: A decision-analytic model and cost-effectiveness analysis. *Int J Technol Assess Health Care* 2005;21(3):351–8.
  - 20 Kemler MA, Furnee CA. Economic evaluation of SCS for chronic reflex sympathetic dystrophy. *Neurology* 2002;59(8):1203–9.
  - 21 Taylor RS, Taylor RJ, Van Buyten JP, et al. The cost effectiveness of SCS in the treatment of pain: A systematic review of the literature. *J Pain Symptom Manage* 2004;27(4):370–8.
  - 22 Namaka M, Gramlich CR, Ruhlen D, et al. A treatment algorithm for neuropathic pain. *Clin Ther* 2004;26(7):951–9.
  - 23 Finnerup NB, Otto M, McQuay HJ, Jensen TS, Sindrup SH. Algorithm for neuropathic pain treatment: An evidence based proposal. *Pain* 2005;118: 289–305.
  - 24 Finnerup NB, Otto M, Jensen TS, Sindrup SH. An evidence-based algorithm for the treatment of neuropathic pain. *Med Gen Med* 2007;9(2):36.
  - 25 Rabin J, Steinhauer M, eds. *Handbook on Human Services Administration*. Boca Raton, FL: CRC Press; 1988.
  - 26 Knox RA. Heart transplants; to pay or not to pay. *Science* 1980;209:570575.
  - 27 Ford PJ, Henderson JM. The clinical and research ethics of neuromodulation. *Neuromodulation* 2006; 9(4):250–2.
  - 28 World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA* 2000;284:3043–5.
  - 29 Zundert JV. Clinical research in interventional pain management techniques: The clinician's point of view. *Pain Pract* 2007;7(3):221–9.
  - 30 Smith TJ, Staats PS, Deer T, et al. Clinical trial of an implantable drug delivery System compared with comprehensive medical management for refractory cancer pain: Impact on pain, drug-related toxicity, and survival. *J Clin Oncol* 2002;20:4040–9.
  - 31 North RB, Kidd DH, Farrokhi F, Piantadosi SA. SCS vs repeated lumbosacral spine surgery for chronic pain: A randomized controlled trial. *Neurosurgery* 2005;56:98–107.
  - 32 Kumar K, Taylor R, Jaques L, et al. SCS versus conventional medical management for neuropathic pain: A multicentre randomized controlled trial in patients with failed back surgery syndrome. *Pain* 2007;132:179–88.