



Psychological and Psychiatric Evaluation of the Spine Pain Patient: An Interface of the Mind/Body Dynamic

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Key Points

- Comprehensive treatment of pain patients involves attention to both primary causes and tributary results.
- The objective and subjective perception of pain are bidirectionally intertwined and influence each other.
- Patients may be confused by this interaction; clinicians who understand the interface will better articulate a treatment strategy.
- Effective empathic communication involves affect more than cognition; at the same time, a clinician should be aware of the risk of personal affective distortion.
- PTSD is a significant co-occurring condition with chronic pain, often misinterpreted as anxiety or depression. The pain clinic encounter may provide a unique opportunity for early treatment of PTSD.
- Substance use disorders and pain influence each other, but there are significant misperceptions about incidence, prevalence, causality, and treatment approaches.
 - Discussing controlled substances can lead to misinterpretations and miscommunication.
 - There are established strategies to best address this comorbidity.
- Suicide risk is increased with chronic pain; it is important to address subtle signs of diminished coping strategies.
- The modern mind-body construct is based on objective observations and should be included in the comprehensive multimodal treatment of spinal pain.

Introduction

Clinicians who are dedicated to treating complex spine pain patients are well aware of the multisystem and interdisciplinary complexity of the cases. Comprehensive treatment of any patient requires awareness and thoughtful considerations of treatment approaches and modalities that extend beyond the idealized scope of management imagined by the provider. The goal of this chapter is to offer the reader practical guidance and insight into some of the behavioral manifestations by patients with a complex pain process including their responses to treatment modalities that are being offered. These behaviors may have primary or secondary mental origins and may or may not fit existing taxonomic or diagnostic criteria according to either the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM). As with most co-occurring conditions, there is a confluence of mechanisms at work, and the integration may not be simple. The mind-body dynamic is a subtle construct. This chapter will help define it and apply this to some of the common concerns pain clinicians voice as they deal with the pain/behavior interface during treatment.

Duality

A highly simplified but useful cornerstone to approach the comprehensive evaluation of a patient presenting with pain is summarized in seven words: *Pain affects mood and mood affects pain*. At first this may seem a simplistic dictum; however, it exemplifies a mind-body dynamic. The bidirectionality is partly a result of the brain's highly associational makeup that invariably compares new and past experiences, both physical and emotional. Moreover, the amount of attention given to these experiences can be viewed as occurring in *top-down* "voluntary" (prefrontal, goal oriented, *endogenous*, or sustained) vs. *bottom-up* "automatic/involuntary"

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(parietal, stimulus generated, *exogenous*, or transient) processes. Although there is evidence that the endogenous and exogenous attention pathways operate independently, the “intertwining” with consciousness and response to stimuli are variable both physiologically as well as perceived [1].

Like other complex physiologic homeostatic systems that constantly maintain a tightly balanced steady state (e.g., autonomic, hemostatic, endocrine, and immune), the pain system employs feedforward and feedback mechanisms to achieve a purposeful and protective functional equilibrium. When this advantageous steady state is disturbed, protective homeostatic systems can become disruptive or even dangerous to the individual.

From the behavioral standpoint, chronic pain patients are dealing with a “pain-trap.” They experience a shift in the protective signaling function of the pain system. Whereas pain typically signals something that is to be changed or avoided, chronic pain exceeds usual duration limits. The patient begins to find themselves unable to make sufficient changes to escape their physical and psychological discomfort. As the attention shifts from exogenous to endogenous, a new quandary presents itself in the duality of frontal-cortical versus striatal (“limbic”) mental processes. Visualize frontal as proactive or executive (judgment, foresight, and planning) and limbic as reactive or reflex. We need both of these systems in order to remain safe and secure as we engage in daily activities. Much of our daytime is spent unconsciously engaged in avoiding harm: we look both ways before crossing, we sidestep suspicious or threatening things, we adhere to rules of the road and sidewalk, and we dress for security with weather appropriate items or bright/reflective sports gear. The limbic system is our early warning system and is very sensitive. The frontal lobes generate managerial oversight for what to do with hazard and are quite specific. *When we are threatened, it interferes with our sense of security, self-esteem, and ambition.* To press on with the concept, chronic pain functionally shifts the density of responses to threats beyond early automatic responses toward more frontal-temporal processing. By recruiting more of our attention pathways, chronic pain interferes with the ideal homeostasis of mind and can influence the physiologic response [2]. The chronic pain process may lead to allosteric compensation in the frontal cortex and influence corticofugal interactions at midbrain and spinal levels [3]. For clinicians who treat pain, understanding this highly encompassing dichotomy manifested by chronic pain will lead to a more sophisticated, comprehensive, and empathic treatment approach.

It is very exciting that there are many recent studies using functional neuroimaging that can illustrate the brain networks responsible for the subjective responses to pain [4]. Neuroimaging studies of psychiatric conditions and observed responses to multimodal treatments are guiding targeted treatments [5]. Our eventual hope is for robust guided

advancements in the understanding and treatment to pain incorporating possible individual differences in emotional modulation of pain neural processing including at the level of the spinal cord and brainstem [6].

Just as I have used the expression “pain-trap” as a concept, any number of conditions can produce a similar scenario: COPD-trap, CHF-trap, addiction-trap, etc. The unifying implication is a significant systems disease that consumes many collateral resources and energy.

Empathy and Countertransference

It would not be reasonable to expect a clinician with expertise and focus on pain management to intuitively perceive and understand behavioral dynamics at the level of a behavioral specialty trained clinician. Medical schools attempt to teach empathy as part of the curriculum, but a recent review identified that the historic metrics of empathy in training may be limiting [7]. Most emphasis has been on cognitive empathy which involves an ability to understand another’s experience and then communicate and confirm that understanding with someone. Affective empathy has more to do with a sense of emotional congruence or feeling about that person’s experience. The blending of cognitive and affective empathy will more likely yield the goal of perceiving a patient’s emotional state and couple it with a motivation to address their welfare. Patients often express a wish to feel heard or be understood more than to be investigated. A patient is a complex being with hopes, wishes, and dreams as well as hurts, regrets, and fears. In modern clinical settings with demands to meet relative value units (RVU), see more patients, and attend to the electronic medical record (EMR), trying to “relate emotionally” with a patient sufficiently may seem a tall order. In a twist on the “mind-body dynamic” interface, there are some practical things the clinician can consider in generating a sense of congruence and collaboration in their patient’s care including posture and taking short spans of time away from the EMR [8]. Consider taking the time to identify and develop the “soft skills” that will enhance your clinician-patient interaction and conceivably even impact patient outcome positively [9]. Think about this as you complete your next new evaluation, for example.

Psychiatry and psychology training puts a significant emphasis upon self-awareness regarding the impact a clinician has on the patient. One entity that is accentuated in training as a potential problem emotion in the treater is the concept of *countertransference*, which addresses the reactions and responses the treater has toward the patient based on the treater’s own background and personal issues. Specifically, the priority here is placed on the trainee understanding *their own* response to the patient, good or bad. This is important to avoid accidentally pursuing a path in which the clinician is

making decisions on behalf of the patient while influenced by their own emotions. If we seek to put emphasis on shared decision-making for patients seeking help with complex medical problems, we have to keep an emphasis on patient-centered “decision quality” [10–12]. Our own mind-body dynamic affects our impact on our patients.

Post-traumatic Stress Disorder (PTSD)

PTSD may be one of the most clinically overlooked co-occurring psychiatric diagnoses in chronic pain management [13]. Although the type of pain linked to PTSD is variable, a large-scale systematic review showed a consistent association between chronic pain and PTSD [14]. From a treatment perspective, it is worthwhile to imagine two types of patient when considering PTSD and pain. Patients who have had PTSD exposure and symptoms *before* the onset of an index pain event have primary PTSD, which I will call PTSD1; those who develop PTSD from an index pain event and the sequelae following pain onset have secondary PTSD, which I will call PTSD2. In either case, there will be clinical presentations that are manifest because the “duality,” or interplay (intertwining), of the physical and mental responses to pain and trauma.

In the most recent DSM-5, which is the standard classification of mental disorders used by mental health professionals in the United States, PTSD is now categorized under *trauma and stressor-related disorders* and not under the anxiety disorders [15]. The diagnosis complex includes the exposure event(s) “A” and sequelae “B–E.” Exposure (A) includes actual or threatened, death, serious injury, or sexual violence: the previous language that “involves fear, helplessness, or horror” is no longer included acknowledging that dissociation can occur at the time of the event. The requirement of exposure to a stressful event as a precondition for the diagnosis is particular among psychiatric disorders.

The PTSD persisting clinical sequelae (B–E) include:

- B. Intrusion symptoms: involuntary recall, nightmares, flashbacks, distress, and marked physiologic reactivity
- C. Persistent avoidance of stimuli associated with the trauma: reminders, thoughts, or feelings
- D. Negative alterations in cognitions and mood that are associated with the traumatic event: dissociative amnesia (loss of memory of key features), persistent negative self-beliefs and/or distorted blame of self or others for causing the traumatic event or for resulting consequence, loss of interest, detachment/estrangement, and constricted affect
- E. Alterations in arousal and reactivity that are associated with the traumatic event: irritability, aggressivity, recklessness, hypervigilance, startle, poor concentration, and sleep disturbance

DSM-5 spectrum diagnosis allows clinicians more flexibility to account for variations from person to person [15]. Upon review of the above set of diagnostic criteria, the pain clinician will likely recognize any number of these traits in their patients. By becoming more attentive to the mechanism behind what may be perceived as disruptive behaviors by the patient, the clinician can more accurately diagnose co-occurring conditions that produce the patient’s pain presentation.

PTSD is associated with high degrees of depression and/or anxiety. It is important to remember that clinicians may be more attuned to recognizing depression and anxiety while overlooking PTSD as the primary diagnosis. Sometimes the presentations of PTSD may even invoke diagnosis such as “bipolar,” “borderline,” and “psychosomatic.” There is ample evidence that patients may respond to treatment modalities to diminish depression and anxiety symptoms, while PTSD symptoms may still linger [16].

It would be propitious to put more emphasis on identifying patients who demonstrate PTSD2. In cases of PTSD2, the Pain Clinic evaluations can serve as an excellent opportunity for a primary, accurate diagnosis that could generate prospects for early and more rigorous treatment of co-occurring PTSD in this group. This may mitigate penetrating and persisting PTSD symptoms that could interfere with comprehensive multimodal pain treatments offered to the patient [17].

Earlier in this chapter, the concepts of duality and attention put emphasis on the response of the chronic pain patient to vulnerability. PTSD symptoms are associated with high catastrophizing (see PTSD symptoms “E”) resulting in low self-efficacy. Efforts to overcome fear-related beliefs (kinesophobia and avoidance) by tailoring interventions may motivate patients’ perceptions to be more engaging in rehabilitative activities [18]. From a practical standpoint, if the clinician is able to shift thinking from “why is this patient behaving this way?” (possibly pejorative) to “what is behind the patient behaving this way?” (empathic and solution oriented) one may circumvent a clinical lost opportunity.

Controlled Substances and Substance Use Disorder (SUD)

The linkage between chronic pain and SUD is bidirectional [19]. It is beyond the scope of this chapter to address the scientific epidemiology of this confluence; however, in terms of the mind/body dynamic, the interaction of perceived pain vs. sought relief invokes the internal and external neurobehavioral interactions discussed earlier in this chapter.

The rubric of controlled substances prescription (CSRx) arises often with chronic pain patients and can become complex for any number of reasons including historic prescribing patterns, response or failure to attempted treatment modalities, and possible (likely) misinterpretations of treatment

application and results on the part of the patient or clinician. The recent confluence of analgesic prescribing trends and recent focus on the “opioid crisis” [20] has resulted in polarization of attitudes by stakeholders surrounding CSRx. Negotiating this prescribing theme can invoke many prefrontal and striatal neurobehavioral circuits and responses in both clinicians and patients. It is important to be mindful about making conscious or unconscious affiliations of CSRx use to substance use disorder (SUD) with either prophylactic or prejudicial intent. To make matters worse, the language of SUD can be confusing. Notably, clinician CSRx decisions can be influenced by menaces of legal sanction [21].

It will be useful at this juncture to draw out some presuppositions. The history of addictions has been steeped in stigmatic language worldwide [22]; within the modern field of addiction medicine and addiction psychiatry, there is great emphasis placed on the language surrounding addiction so as to avoid stigma. Here are some useful key terms:

- I. Tolerance: diminished response to a drug, which occurs when the drug is used repeatedly and the body adapts to the continued presence of the drug
- II. Dependence: adaptive changes by the body to a drug that result in *withdrawal symptoms upon cessation of that drug*
- III. Addiction: compulsive drug seeking despite negative consequences (NIDA); impaired control, social impairment, risky use, and *craving* leading to problematic pattern of use of an intoxicating substance with clinically significant impairment or distress (2 of 12 DSM V criteria) [15]
- IV. Abuse = illegal patterns: selling, forging prescriptions, stealing drugs from others, using by nonprescribed route (e.g., injecting or crushing and snorting), multiple doctor sources or multiple pharmacy fills, repeated losing/running out/self-dosage increases
- V. Misuse: nonpatterned use of illicit substances or incorrect use of CSRx

Engaging the patient in a discussion about CSRx while avoiding interactive pitfalls can be a significant challenge. A suggested approach is to avoid dichotomous language and focus on solving any *misinterpretations* that may be had by the patient or the clinicians. If a patient says they took some extra tablets, consider asking an open-ended question such as “how did you decide to do that?” rather than a closed-ended “why did you do that?” (the response will invariably begin with “because...”).

Consider trying a spectrum (non-dichotomous) approach to address the subject with the patient (Fig. 10.1).

Focus attention on the colored triangle suggesting it is like a stoplight: Green is *go*, yellow is *proceed with caution*, and red is *stop*. Explain that CSRx is complicated by the fact that these medications may work favorably at low doses, but

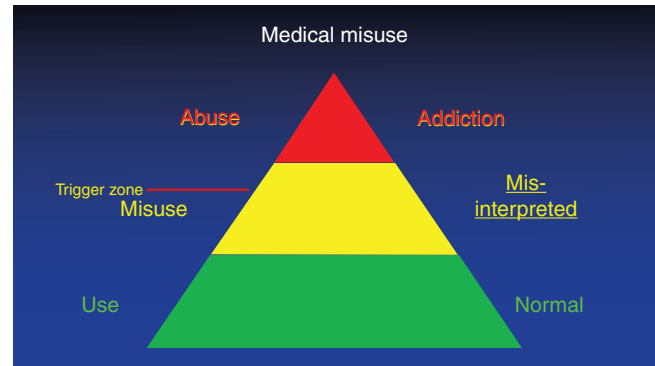


Fig. 10.1 Diagram tool to guide the controlled substances prescription (CSRx) dialogue toward solution and away from confrontation by using an easily recognizable construct (see text) [23]

as one increases dose, unwelcome neurobiological responses including triggering of tolerance and dependence occurs and can lead to reward, addiction [24], or overdose. Keep most of the emphasis on the yellow zone and the word *misinterpreted* to keep the clinician and patient on a collaborative plane. If the issue is weaning a patient down from a high morphine equivalent (or benzodiazepine) dose, suggest that the patient strive “to move towards the green zone.” The Trigger zone is meant to indicate that as doses increase, there is increased risk of invoking anticipation and preoccupation for use. There is ample scientific evidence that CSRx risk can outweigh benefit on many levels [25]; communicating this to a chronic pain patient in a non-shaming way will yield the best results.

Note the term *trigger zone* in the above illustration. This represents a proposed mechanism of shift to increased sensitization (“trigger” or runaway) response to a potent drug [26].

A treatment trap to avoid is concluding a patient with any history of SUD as ineligible for CSRx. Although a previous history of SUD is considered an additive risk for future SUD, it is not exclusive. Assessment of a patient’s recovery status by a skilled addictions specialist can provide useful guidance beyond formulaic opioid risk stratification instruments by addressing psychosocial history and generating a more robust assessment, structure, and monitoring program [27]. The US Substance Abuse and Mental Health Services Administration (SAMHSA) produces a series of Treatment Improvement Protocol (TIP) publications that can assist clinicians in comprehensive decision-making in this setting (Fig. 10.2) [28].

Suicide

Suicide was the 10th leading cause of death in the United States with 44,965 deaths in 2016 at a rate of 13/5 deaths per 100,000 people, half of which were by firearms [29]. A

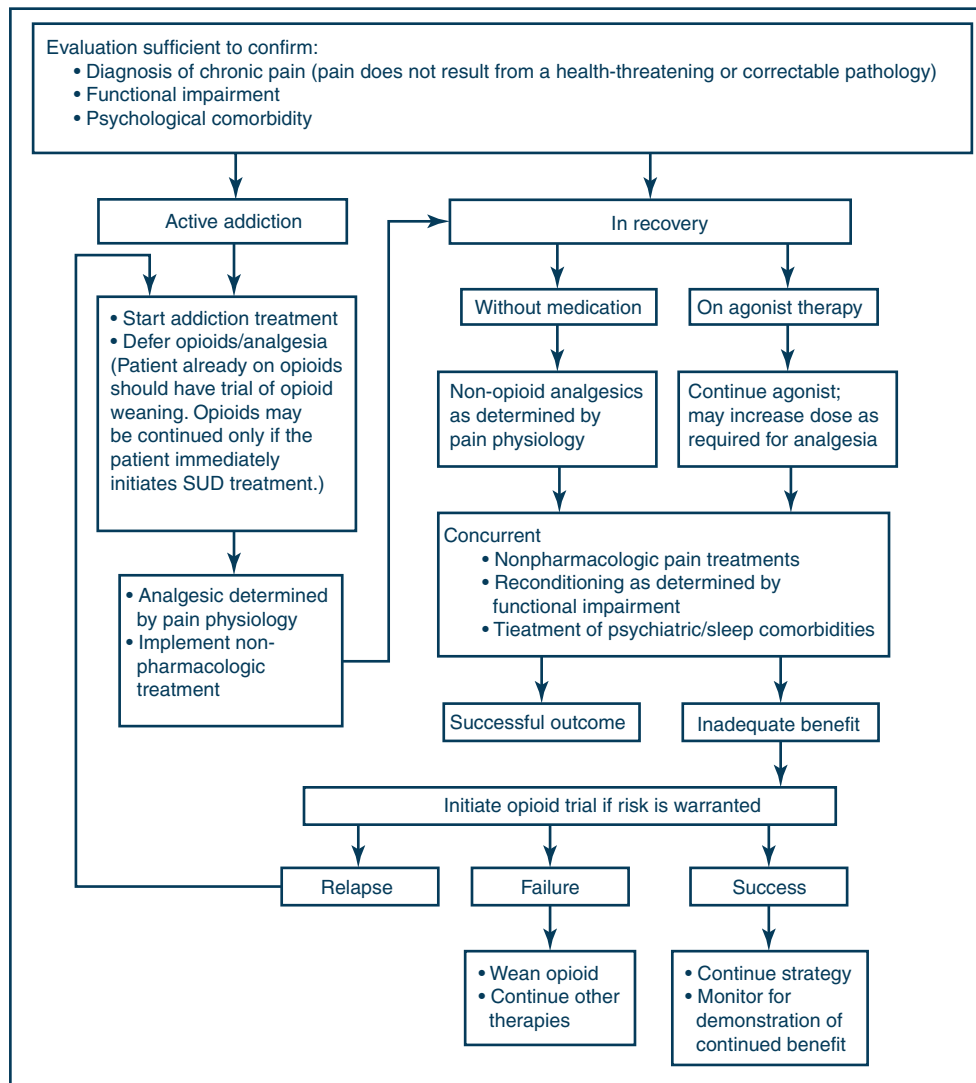


Fig. 10.2 Example of a diagnostic algorithm that guides clinicians who wish to consider opioids in chronic pain patients with SUD history from Protocol (TIP) Series 54. (SMA) 12-4671 Exhibit 4-11 Exit Strategy, p. 62

recent analysis of National Violent Death Reporting System (NVDRS) data from 2003 to 2014 revealed that 8.8% of decedents had chronic pain but was surprising to show an increased death rate trend of those with chronic pain from 7.4% in 2003 to 10.2% in 2014 [30]. A recent comprehensive review of chronic pain and suicide risk corroborated data suggesting that chronic pain is a significant independent risk factor for suicidality [31]. Family history, childhood and adult adverse events, and co-occurring primary mental illness including SUD were considered a general risk with unemployment and disability recognized as an associated risk for suicide for those with chronic pain. Predictors of suicidality included frequent episodes of intermittent pain, sleep problems, and negative perceived mental health, while pain duration, intensity/severity, or type were not related to suicide risk. A note of optimism was generated in the study

by identifying psychosocial risks that are known to be amenable to treatment interventions such as belongingness, burdensomeness, catastrophizing, hopelessness, and mental defeat.

From the mind-body dynamic standpoint, there is noteworthy evidence that central pain processing pathways resemble and/or utilize the same reward/anti-reward pathways as with substance use and other mental disorders [32]. Notable negative behavioral hallmarks occurring with extremes of SUD, pain, depression, and anxiety are significant isolation and withdrawal. The result is diminished suitable coping strategies and can lead to apathy, anhedonia, and numbing. These represent neuropsychopathological allostatic results of the illness.

In the clinical domain, pain specialists should not avoid discussing the emotional restrictions experienced by their

patients. Do not be afraid to ask about suicide; use it as a metric of emotional pain intensity. The report of levels of mild passive (“OK if I didn’t wake up”), moderate passive (“wish I would die”), active consideration (“hope I don’t live) to active (plan, intent and means) is an indication of the burden of emotional hopelessness and mental defeat realizing these are treatable. As the intensity of these negative perceived mental health symptoms intensifies, the clinicians’ response should be to increase emphasis on alternative multimodal therapeutic interventions. It may indicate the need for an assessment by a mental health specialist.

Therapeutic Constructs

The mind-body construct has a long history dating back to Buddha, Aristotle, and Plato and has undergone philosophical, theological, metaphysical, and mystical examination and dissertation. The goal of this chapter has been to offer pain clinicians an objective and scientific introduction to contemporary mind-body constructs with clinically applicable examples. The intention is to expand the treaters therapeutic contribution, thus amplifying the likelihood of a favorable outcome. Modern mind-body practice mechanism studies objectively demonstrate recruitment of genetic, neuroplastic, hormonal, and homeostatic effects [33]. The ultimate goal is to identify modalities that demonstrate clear clinical or physiological benefit. A good example of this is a study of modulation of pain through mindfulness meditation using fMRI with the added practical observation of seeing effect within four sessions [34]. A recent and pertinent article that proposes “addiction as learning, not disease” is highly informative and provides a perspicacious angle on how to consider pain behaviors [35].

The benefit of psychiatric and psychological expert evaluation and input cannot be emphasized. Through collaborative exchange of specialty knowledge, predictive assessments can be made in specific pain treatment areas such as the decision tree for spinal cord stimulator placement [36].

References

- Pinto Y, van der Leij A, Sligte I, Lamme V, Scholte H. Bottom-up and top-down attention are independent. *J Vis.* 2013;13(3):16. <https://doi.org/10.1167/13.3.16>.
- Crofford L. Chronic pain: where the body meets the brain. *Trans Am Clin Climatol Assoc.* 2015;126:167–83.
- Ong W, Stohler C, Herr D. Role of the prefrontal cortex in pain processing. *Mol Neurobiol.* 2019;56(2):1137–66. <https://doi.org/10.1007/s12035-018-1130-9>.
- Lin Q, Li L, Liu J, Liu W, Huang G, Zhang Z. Influence of individual differences in fMRI-based pain prediction models on between-individual prediction performance. *Front Neurosci.* 2018;12:569. <https://doi.org/10.3389/fnins.2018.00569>.
- Stern S, Linker S, Vadodaria K, Marchetto M, Gage F. Prediction of response to drug therapy in psychiatric disorders. *Open Biol.* 2018;8(5):180031. <https://doi.org/10.1098/rsob.180031>.
- McIver T, Kornelsen J, Stroman P. Functional MRI reveals emotional modulation of pain processing in the human cervical spinal cord and brainstem. *J Phys Med.* 2018;1(1):10–23.
- Smith K, Norman G, Decety J. The complexity of empathy during medical school training: evidence for positive changes. *Med Educ.* 2017;51(11):1146–59. <https://doi.org/10.1111/medu.13398>.
- Gupta A, Harris S, Naina H. The impact of physician posture during oncology patient encounters. *J Cancer Educ.* 2015;30(2):395–7. <https://doi.org/10.1007/s13187-015-0807-2>.
- Kelley JM, Kraft-Todd G, Schapira L, Kossowsky J, Riess H. The influence of the patient-clinician relationship on healthcare outcomes: a systematic review and meta-analysis of randomized controlled trials. *PLoS One.* 2014;9(4):e94207. <https://doi.org/10.1371/journal.pone.0094207>.
- Barry MJ, Edgman-Levitan S. Shared decision making — the pinnacle of patient-centered care. *N Engl J Med.* 2012;366:780–1. <https://doi.org/10.1056/NEJMp1109283>.
- <http://www.dartmouth.edu/~cecs/siipc/>, https://med.dartmouth-hitchcock.org/csdm_toolkits.html.
- <https://www.massgeneral.org/decisionsciences/>.
- Akhtar E, Ballew A, Orr W, Mayorga A, Khan T. The prevalence of post-traumatic stress disorder symptoms in chronic pain patients in a tertiary care setting: a cross-sectional study. *Psychosomatics.* 2018. pii: S0033-3182(18)30414-6. <https://doi.org/10.1016/j.psym.2018.07.012>.
- Fishbain D, Pulikal A, Lewis J. Chronic pain types differ in their reported prevalence of post-traumatic stress disorder (PTSD) and there is consistent evidence that chronic pain is associated with PTSD: an evidence-based structured systematic review. *Pain Med.* 2017;18(4):711–35. <https://doi.org/10.1093/pm/pnw065>.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Section II: diagnostic criteria and codes, trauma- and stressor-related disorders, posttraumatic stress disorder. Arlington: American Psychiatric Association; 2013. p. 271–80.
- Kessler R, Aguilar-Gaxiolab S, Alonso J, Benjet C, Bromet G, Cardoso G, et al. Trauma and PTSD in the WHO world mental health survey. *Eur J Psychotraumatol.* 2017;8(sup5):1353383. <https://doi.org/10.1080/20008198.2017.1353383>.
- Morasco B, Lovejoy T, Lu M, Turk D, Lewis L, Dobscha S. The relationship between PTSD and chronic pain: mediating role of coping strategies and depression. *Pain.* 2013;154(4):609–61. <https://doi.org/10.1016/j.pain.2013.01.001>.
- Giummarra M, Casey S, Devlin A, Ioannou L, Gibson S. Co-occurrence of posttraumatic stress symptoms, pain, and disability 12 months after traumatic injury. *Pain Rep.* 2017;2(5):e622. <https://doi.org/10.1097/PR9.0000000000000622>.
- Hser Y, Mooney L, Saxon A, Miotto K, Bell D, Huang D. Chronic pain among patients with opioid use disorder: results from electronic health records data. (NIH funded). *J Subst Abuse Treat.* 2017;77:26–30. <https://doi.org/10.1016/j.jsat.2017.03.006>.
- <https://www.cdc.gov/drugoverdose/pdf/pubs/2017-cdc-drug-surveillance-report.pdf>, <https://www.cdc.gov/drugoverdose/epidemic/index.html>.
- Dineen K, Bubeck J. Between a rock and a hard place: can physicians prescribe opioids to treat pain adequately while avoiding legal sanction? *Am J Law Med.* 2016;42(1):7–52.
- Corrigan P, Schomerus G, Shuman V, Kraus D, Perlick D, Harnish A, et al. Developing a research agenda for understanding the stigma of addictions Parts I and II: lessons from the mental health stigma

- literature. *Am J Addict*. 2017;26(1):59–74. <https://doi.org/10.1111/ajad.12458>, <https://doi.org/10.1111/ajad.12436>.
23. Acampora G. Massachusetts General Hospital. PowerPoint presentation, rev. 2019.
 24. Koob G, Volkow N. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry*. 2016;3(8):760–73. [https://doi.org/10.1016/S2215-0366\(16\)00104-8](https://doi.org/10.1016/S2215-0366(16)00104-8).
 25. Jamison R, Mao J. Opioid analgesics. *Mayo Clin Proc*. 2015;90(7):957–68. <https://doi.org/10.1016/j.mayocp.2015.04.010>.
 26. Volkow N, Koob G, McLellon T. Neurobiologic advances from the brain disease model of addiction. *N Engl J Med*. 2016;374:363–71. <https://doi.org/10.1056/NEJMr1511480>.
 27. Jovey R. Opioids, pain and addiction – practical strategies. *Br J Pain*. 2012;6(1):36–42. <https://doi.org/10.1177/2049463712439132>.
 28. Substance Abuse and Mental Health Services Administration. Managing chronic pain in adults with or in recovery from substance use disorders. Treatment Improvement Protocol (TIP) Series 54. HHS Publication No. (SMA) 12-4671. Rockville: Substance Abuse and Mental Health Services Administration, 2011. Exhibit 4-11 Exit Strategy, p. 62.
 29. <https://www.cdc.gov/vitalsigns/suicide/index.html>.
 30. Petrosky E, Harpaz R, Fowler K, Bohm M, Helmick C, et al. Chronic pain among suicide decedents, 2003 to 2014: findings from the national violent death reporting system. *Ann Intern Med*. 2018;169(7):448–55. <https://doi.org/10.7326/M18-0830>.
 31. Racine M. Chronic pain and suicide risk: a comprehensive review. *Prog Neuro-Psychopharmacol Biol Psychiatry*. 2018;87(Pt B):269–80. <https://doi.org/10.1016/j.pnpbp.2017.08.020>.
 32. Elman I, Borsook D, Volkow N. Pain and suicidality: insights from reward and addiction neuroscience. *Prog Neurobiol*. 2013;109:1–27.
 33. Tellas S, Gerbard P, Kozasa E. Physiological effects of mind and body practices. *Biomed Res Int*. 2015. <https://doi.org/10.1155/2015/983086>.
 34. Zeidan F, Martucci K, Kraft R, Gordon N, McHaffie J, Coghill R. Brain mechanisms supporting modulation of pain by mindfulness meditation. *J Neurosci*. 2011;31(14):5540–8. <https://doi.org/10.1523/JNeurosci.5791-10.2011>.
 35. Lewis M. Brain change in addiction as learning, not disease. *N Engl J Med*. 2018;379:1551–60. <https://doi.org/10.1056/NEJMr1602872>.
 36. Paroli M, Bernini O, De Carolis G, Tollapi L, Bondi F, Martini A, et al. Are multidimensional pain inventory coping strategy profiles associated with long-term spinal cord stimulation effectiveness? *Pain Med*. 2018;19(5):1023–32. <https://doi.org/10.1093/pm/pxn106>.