

New Chronic Pain Treatments in the Outpatient Setting: Review Article

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Abstract Chronic pain is an issue encountered by many health care providers in their routine clinical practice. In addition to generalized patient suffering, this condition has significant clinical, psychological, and socioeconomic impact due to its widespread occurrence. The landscape of chronic pain management has been changing rapidly with an array of treatment innovations, better understanding of established therapies, and care coordination across specialties. In this article, we have reviewed emerging new modalities as well as transformation of established therapies by interventional, pharmacologic, rehabilitative, psychological, complimentary, and interdisciplinary approaches.

Keywords Chronic pain · Outpatient · Interventional · Pharmacology · Multidisciplinary · Epidural · Opioids ·

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Neuromodulation · Neuroablation · Regenerative medicine · Psychotherapy

Introduction

Chronic pain is a major cause of suffering, disability, lost productivity, and diminished quality of life. Cross-sectional studies have revealed chronic pain prevalence of up to 55 % in adults. A significant percentage of pediatric patients also suffer from at least one episode of acute pain, which can have similar effects as in adults. In its 2011 report *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*, the Institute of Medicine (IOM) estimated that the prevalence of chronic pain is greater than the combined prevalence of heart disease, cancer, and diabetes, which results in associated medical cost and lost productivity of an estimated \$600 billion [1].

A majority of chronic pain patients are managed in the outpatient setting. Additionally, new fast-track surgical protocols and emphasis on reducing surgical costs have resulted in an increased volume of patients with acute or sub-acute post-operative pain issues being referred to outpatient pain practices. Pain medicine has come a long way since World War II, when John Bonica first proposed the concept of multimodal and multidisciplinary management of chronic pain. This is an exciting period for chronic pain management, and large strides are being made in therapeutic innovation, research, education, and awareness of chronic pain conditions.

We have searched PubMed for all reports published in any language between the first of January, 2013 and November (third week) of 2015 using the following key words: pain medicine, pain management and outpatient. We have focused on the articles related to chronic pain management in the outpatient setting. After reviewing titles and abstracts, we

acquired full-text papers where appropriate. We included systematic reviews, randomized controlled clinical trials, observational studies, expert opinions, and guidelines. We have presented relevant materials in the following categories of chronic pain treatment: interventional pain management, pharmacological management including topical treatments, physical medicine and rehabilitation, pain psychology, and interdisciplinary approaches. We have also discussed innovations and recent research in complimentary and alternative treatments, utilization of informational technologies in treatment of chronic pain as well as new developments in assessment of cost-effectiveness of chronic pain therapies. In addition to new developments, we have also tried to highlight the changing paradigms in pain medicine such as newer indications or transformation of previous treatments and current controversies surrounding established therapies. We believe this is important to address, as these changes determine real world practice of chronic pain.

Interventional Procedures

Neuromodulation

Neuromodulation has established itself firmly as a treatment modality for various chronic pain conditions since the 1960s. Recent advances in this field have led to use of novel programming parameters and newer stimulation targets within the central and peripheral nervous system. The Senza-RCT randomized controlled trial is a multicenter study that demonstrated superior results from high-frequency stimulation, up to 10 kHz as compared to conventional spinal cord stimulation (SCS) for the treatment of back and leg pain. Moreover, this high-frequency stimulation is paresthesia-free, and epidural lead placement is based on anatomic landmarks rather than paresthesia mapping [2••]. Early results from the ACCURATE study have shown superiority of dorsal root ganglion stimulation (DRG) to conventional SCS in the treatment of lower extremity CRPS and neuropathic pain. Here, the epidural leads are positioned in proximity to the dorsal root ganglion of the relevant level in the spinal cord. This technique had fewer postural variations in stimulation pattern and lesser paresthesia in undesired areas [3]. Burst stimulation and sub-threshold high-density stimulation are also currently being investigated.

Vagal nerve stimulation was traditionally used for treatment of refractory epilepsy and depression. Promising results have been noted from vagal nerve stimulation (VNS) in acute/chronic migraine, acute/chronic cluster headaches, fibromyalgia, and pelvic pain [4]. Non-invasive VNS has shown efficacy for migraines and cluster headaches. High-safety profile and ease of use make it an attractive modality for this disabling pain condition [5].

Neuro-ablative Techniques

Radio-frequency Ablation

Cooled radio frequency (RF) ablation is relatively new as compared to thermal (hot) radio frequency ablation (RFA). The temperature at the tip of the needle is actively cooled by internal irrigation, which permits a larger sized lesion to be performed and potentially improves success rates. Peripheral joints such as hip, knee, and the sacroiliac joints can have variable sensory innervation and hence, cooled RF can potentially give better results from the neurotomy procedure. Cooled RF has shown benefit in patients with sacroiliac joint pain and knee pain [6]. Additionally, trigeminal neuralgia (TN) is a relatively common and extremely painful condition in which RF can be useful. Percutaneous RFA of TN through foramen ovale is well-described and commonly used in clinical practice. A novel percutaneous approach through the foramen rotundum to specifically target maxillary branch of the TN was investigated in patients with isolated TN of the maxillary branch and found to be safe and effective [7].

Cryoablation

Cryoablation has been in use for long as a means of controlling pain of peripheral nerve origin. Recent advances have been made in this technology, which permits use of much smaller gauge needles and a portable device. This can result in an improved patient comfort, an easier setup, and training of personnel involved. A recent case series by Bellini et al demonstrated utility of cryoneurolysis for lumbar facet pain, knee pain, and sacroiliac pain [8].

Regenerative Medicine Techniques in Treatment of Chronic Pain

Prolotherapy

Prolotherapy involves the injection of dextrose solution or other irritant substance into joint/tendon/soft tissue in an effort to provoke healing tissue response. The clinical efficacy of Prolotherapy remains a subject of debate. A recent systematic review supported clinical efficacy of prolotherapy injections in lower limb tendinopathies and fasciopathy [9]. There is still little evidence to determine the proper dose, concentration, or frequency for effective treatment measures.

Platelet-rich Plasma (PRP)

Similarly, injections of platelet-rich plasma (PRP) have become very popular for treatment of tendon or sports injuries. A meta-analysis showed some benefit for PRP in the intermediate long-term duration (36 months) compared to local

anesthetics, physical therapy, steroids, or autologous blood [10]. However, the studies were variable in terms of treatment protocol, comparators, and duration of follow-up. One study showed promising results when PRP was compared with PT in chronic partial supraspinatus tears [11]. Intra-articular injection of PRP was found to be an effective and safe method for treatment of mild to moderate, but not severe osteoarthritis (OA) in a recent systematic review [12•].

Controversies Surrounding Established Procedures

Epidural steroid injections (ESI) are commonly performed for lumbosacral radicular pain. Transforaminal ESI have been preferred by a number of pain physicians due to expected greater ventral spread obtained with this technique, but there has been a growing concern about the risks associated with transforaminal ESI injections, especially at the cervical level, and in concordance with the use of particulate steroids due to the potential for catastrophic complications such as vascular injury, stroke, spinal cord infarction, and dissection. Ultrasonography has helped to *prevent* vascular injury rather than *detect* it post factum with fluoroscopy *after* the procedural needle has penetrated the vessel [13]. In contrast to recent preferences for transforaminal epidural steroid injections, a recent study demonstrated that paramedian interlaminar injections are as effective as transforaminal injections for improving pain and functional status in patients with chronic lumbosacral back and radicular pain [14].

The overall efficacy of epidural steroid injections for back pain and radicular pain has been debated for years and recently, this controversy has intensified. Chou et al [15••] published a meta-analysis which concluded that ESIs reduced pain intensity in radiculopathy patients for only a short period. The Agency for Healthcare research and quality (AHRQ) recently released its report on commonly performed spine injections for back pain/radicular pain (based on results of Chou et al) and questioned the efficacy of these treatments [16]. The methodology used for this meta-analysis and patient selection has been questioned and hence, the results of the study cannot be generalized to the current practice of pain medicine. ESIs are a valuable option for certain groups of patients, and more research is mandated to determine the optimal patient groups, type of steroid, drug dosage, and technical aspects of this procedure [17•, 18].

Interventions for Abdominal and Pelvic Pain

Transversus abdominis plane blocks are usually reserved for patients with pain thought to be of somatic origin. Smith et al. described a case series where this block was successfully used for visceral abdominal pain in patients with chronic pancreatitis, Crohn's disease, and pancreatic pseudocyst [19]. Thus, this treatment potentially may be considered for visceral or

somatic origin pain. Interstitial cystitis is a difficult to treat condition and is characterized by persistent irritating micturition symptoms and pelvic pain. Intravesical instillation of dimethyl sulfoxide, BCG, pentosan polysulfate, and hyaluronic acid has been trialed with variable results. High-molecular weight hyaluronic acid was found superior to other instillates in terms of both cost-effectiveness and efficacy [20]. Resiniferotoxin is an experimental drug, similar to capsaicin that is being investigated for interstitial cystitis. Botox injections or Onabotulinumtoxin A injections into perineal muscles has shown long-term beneficial effects in patients with vestibulodynia and perineal pain [21].

Treatment of Postoperative Pain in Ambulatory Settings

In the era of bundled payments and value-based care, there has been increasing emphasis on fast-tracking hospital discharges, reducing readmission rates and improving patient satisfaction, and the involvement of the pain physician provider. This economic and regulatory environment has given inspiration to the concepts of “enhanced recovery after surgery” and the “perioperative surgical home.” Opioid reduction and the use of multimodal therapies for an acute postoperative pain have become the focus of attention. Ambulatory continuous peripheral nerve blocks have emerged as important tools in the armamentarium of anesthesiologists for managing surgical pain and facilitating rehabilitation in this setting [22•]. Other newer effective treatment strategies include instillation of liposomal bupivacaine in the surgical incision or joint [23], oral pregabalin [24], ketamine [25], and some other agents. Preoperative pregabalin decreased opioid consumption and pain scores in the hospital but did not improve pain or physical function at 6 weeks or 3 months after total hip arthroplasty in a recent study [24].

Pharmacologic Treatments

Opioids

Among commonly prescribed pain medications, including non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, muscle relaxants, membrane stabilizers, and topical agents, opioids produce the most controversy. The number of opioid prescriptions has nearly tripled from 1991 to 2013, and with that, morbidity and mortality have also concurrently risen. For example, drug overdose was the most common cause of injury death in 2013; more than half of drug overdose deaths are from prescription drugs, and opioids are the commonest drugs implicated [26].

To prevent opioid abuse, misuse and diversion several state and federal laws have been enforced. Abuse deterrent (AD) opioids are one way of mitigating opioid abuse, but they are

not foolproof. AD opioids may be designed by using physical/chemical barriers, agonist–antagonist combinations, aversion technology, prodrugs, or by controlled delivery methods. A combination of any of the above technologies may also be used. The FDA has released detailed guidelines for designing newer AD opioids. There are currently five analgesics with FDA abuse-deterrent label and several others under review. There has been growing evidence that the use of these formulations is associated with lower incidence of abuse of these drugs [27•].

Chronic opioid therapy is associated with multiple adverse effects; gastrointestinal side effects are the most frequent. Opioid induced constipation (OIC) can be difficult and exasperating for patients. Peripherally acting opioid mu receptor agonists (PAMORAs) have been found effective for refractory OIC that has not responded to dietary changes or laxatives. These drugs are also a safe and effective option for management of OIC during pregnancy [28]. Opioids are commonly used tools in the management of cancer pain. Treatment of breakthrough pain (BTP) in opioid-tolerant cancer patients is challenging. A recent systematic review addressed this issue and found oral transmucosal or intranasal fentanyl formulations to be potent, rapidly effective, and safe for treatment of BTP episodes in this subset of patients [29].

Bisphosphonates

Bisphosphonates are widely used for osteoporosis and other metabolic bone diseases. In five randomized controlled trials, oral and intravenous alendronate and intravenous clodronate, pamidronate, and neridronate demonstrated efficacy in treatment of pain related to CRPS, Type I [30].

Topical Therapies

Compounded topical analgesics have a major attraction due to potentially lower side effects and increased patient compliance. Capsaicin 8 % patch and oral pregabalin have been used for neuropathic pain for quite a few years now. A head to head efficacy and safety trial showed that capsaicin patch provided non-inferior pain relief to an optimized dose of pregabalin but with faster onset of action, fewer systemic side effects, and greater treatment satisfaction [31]. Other combinations have been trialed as well. For example, topical amitriptyline–ketamine combination demonstrated benefits in some studies for peripheral neuropathic pain [32]. However, efficacy may depend on several factors such as choice of the vehicle, concentration, pain site, and specific diseases.

Cannabinoids

A hot topic across the country currently is assessing the legal use of cannabinoids in the United States. Basic science

research has shown endocannabinoids to be part of our natural pain and immune defense network. About 25–30 randomized controlled trials demonstrated significant analgesic effects from the use of cannabinoid derivatives. One of the authors of this paper practices in a state where medical marijuana is legalized and encounters many chronic pain patients who vouch for the pain-relieving benefits of medical marijuana. The recent systematic reviews on this topic support a modest analgesic benefit from cannabinoids [33]. The long-term effects from the increasing use of these compounds remains to be seen.

Physical Medicine and Rehabilitation

There has been a growth of physical therapy techniques and devices trialed for chronic pain conditions in the past decade. Management of pain associated with knee osteoarthritis (OA) has been investigated fairly extensively, due to its high prevalence. Resistance exercises and therapeutic ultrasound were shown in meta-analyses to reduce pain, alleviate stiffness, and improve physical function in these patients [34]. Another study demonstrated prolonged benefit from the use of transcutaneous electrical nerve stimulation (TENS) for knee OA [35]. The trial of a low-intensity ultrasonic device on the affected body part was found to be safe and feasible for treatment of tendinopathies of the elbow and ankle [36].

Noxipoint therapy (NT) is a novel form of electrotherapy, where brief jolts of energy are applied precisely between the two insertion sites of a muscle. Each participant received three to six 90-min sessions of NT or conventional PT and TENS. NT improved pain scores and quality of life at follow-up, up to 5 months [37•]. Diabetic peripheral neuropathy is a common complication from diabetes mellitus, and medication is not always effective controlling the pain symptoms. Low-energy laser therapy was found to be an effective diabetic peripheral neuropathy in an observational study [38].

Psychotherapy

Psychotherapy techniques have clinical utility in the context of chronic pain due to the multifactorial etiology of pain. We would like to put the spotlight on a few psychotherapy modalities that have shown positive results in the recent studies. “Mindfulness meditation” reduced pain intensity and pain unpleasantness and caused greater activation in the brain regions associated with cognitive modulation of pain. The use of functional neuroimaging to demonstrate the benefits of this therapy may foster greater acceptance of this as a legitimate pain treatment [39•]. “Mindfulness-based stress reduction” was shown to be a feasible alternative for back pain in another study [40].

Multidisciplinary Strategies

Chronic pain has multifactorial etiology and can be best addressed by using a multipronged approach and collaboration between specialists. Recent studies lend further support to multidisciplinary treatment of chronic pelvic pain, pain management in pregnancy, cancer pain, and chronic pain in post lumbar spine surgery patients [41, 42]. These studies focused on the use of specialized pain group therapies, pharmacologic and non-pharmacologic approaches, physical therapy, graded motor imagery, cognitive behavior therapy, self-management support, pain science education, and complementary and alternative medicine techniques for management of chronic pain in outpatient settings. This kind of interdisciplinary approach improves pain, disability, mood, and physical function outcomes.

Complimentary and Alternative Medicine

We identified a number of studies addressing the use of complimentary and alternative medicine (CAM) in chronic pain settings. Yoga intervention resulted in a decreased pain, stiffness, and swelling in OA patients, but physical function and psychosocial well-being were inconclusive [43]. Moderate pressure massage therapy was found effective increasing range of motion and lessening pain and sleep disturbances in knee OA. A meta-analysis concluded that the Chinese herbal bath therapy is safe, effective, and a simple alternative treatment modality for knee arthritis [44]. Integrative medicine, which combines CAM and conventional treatments for low back pain, was found to have beneficial effects on pain and function [45].

Digital Technologies

The world of the Internet revolution, smartphone apps, and gaming gadgets has had an impact on care of chronic pain patients. The use of interactive gaming consoles was associated with greater reduction in patients during minor burn rehabilitation [46]. A newly registered trial aims to assess if the addition of an app delivered relaxation to progressive muscle relaxation is superior to conventional relaxation techniques [47]. New technologies and apps can also be used to guide physicians and health care providers in making treatment decisions.

Cost-Effectiveness of Treatment Modalities

The current socioeconomic and political climate mandates health care providers to consider cost issues in the overall picture of patient care and management. Low back pain is the commonest chronic pain condition in the USA. Kazberouk et al [48•] conducted a survey of organizations that

were involved in bundled care payments for spine care and surgery. Several of these organizations expected 30–45 % of their spine volume to be covered under bundled payments in the next 3 years. Their reasons for moving to bundled care were increased patient volume, surgical yield, and financial benefits from improved efficiency. Another study that might guide clinical management protocols involved knee OA patients. They concluded that in patients with multiple comorbidities, naproxen- and ibuprofen-containing regimens are more effective and cost-effective than opioids for knee pain [49].

Conclusion

Chronic Pain is a common condition encountered by health care providers across a multitude of specialties. Since the effects of chronic pain are palpable in multiple dimensions of patients' life, their families, and communities, it is important that physicians and others in the health care sector be aware and be equipped to manage chronic pain. Traditionally, pain has been undertreated and underrecognized but it is encouraging to see new developments in the field of pain management in recent years. This review highlighted some important innovations and refinements in outpatient chronic pain management using a comprehensive outlook. We encourage healthcare providers reading this chapter to analyze and share their experience to help other medical professionals to achieve the best possible clinical outcomes.

Compliance with Ethical Standards

Conflict of Interest Radhika Grandhe, Dmitriy Souzdalnitski, and Karina Gritsenko declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Relieving pain in America: a blueprint for transforming prevention, care, education and research. 2011. iom.nationalacademies.org/reports/2011/relieving-pain-in-america-a-blueprint-for-transforming-prevention-care-education-research.aspx. Accessed 30 Nov 2015.
2. Kapural L, Yu C, Doust MW, et al. Novel 10-kHz high-frequency spinal cord stimulation for the treatment of chronic back and leg pain. *Anesthesiology*. 2015;123(4):851–60. **Multicenter**,

- randomized controlled pivotal trial showing non inferiority and superiority of high frequency SCS compared to conventional stimulation for a common pain condition. This modality allows paresthesia free stimulation.**
3. A Safety and Effectiveness Trial of Spinal Cord Stimulation of the Dorsal Root Ganglion for Chronic Lower Limb Pain (ACCURATE). In: A Safety and Effectiveness Trial of Spinal Cord Stimulation of the Dorsal Root Ganglion for Chronic Lower Limb Pain. 2013. <https://clinicaltrials.gov/ct2/show/nct01923285>. Accessed 6 Dec 2015
 4. Chakravarthy K, Chaudhry H, Williams K. Review of the uses of vagal nerve stimulation in chronic pain management. *Curr Pain Headache Rep.* 2015;19(12):54.
 5. Yuan H, Silberstein SD. Vagus nerve stimulation and headache. *Headache.* 2015 doi: 10.1111/head.12721. [Epub ahead of print]
 6. Salmasi V, Chaiban G, Eissa H et al. Application of cooled radiofrequency ablation in management of chronic joint pain. *Tech Reg Anesth Pain Manag.* 2015; doi: 10.1053/j.trap.2015.10.013
 7. Xue T, Yang W, Guo Y, et al. 3D Image-guided percutaneous radiofrequency thermocoagulation of the maxillary branch of the trigeminal nerve through foramen rotundum for the treatment of trigeminal neuralgia. *Medicine (Baltimore).* 2015;94(45), e1954.
 8. Bellini M, Barbieri M. Percutaneous cryoanalgesia in pain management: a case-series. *Anaesthesiol Intensive Ther.* 2015;47:131–3.
 9. Sanderson LM, Bryant A. Effectiveness and safety of prolotherapy injections for management of lower limb tendinopathy and fasciopathy: a systematic review. *J Foot Ankle Res.* 2015;8:60. doi:10.1186/s13047-015-0117-2.
 10. Andia I, Latorre PM, Gomez MC, et al. Platelet-rich plasma in the conservative treatment of painful tendinopathy: a systematic review and meta-analysis of controlled studies. *Br Med Bull.* 2014;110(1): 99–115.
 11. Ilhanli I, Guder N, Gul M. Platelet-rich plasma treatment with physical therapy in chronic partial supraspinatus tears. *Iran Red Crescent Med J.* 2015;17(9), e23732.
 12. Meheux CJ, Mcculloch PC, Lintner DM et al. Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: a systematic review. *Arthroscopy.* 2015; doi: 10.1016/j.arthro.2015.08.005. **Platelet-rich plasma injection is an emerging technique in the non operative management of pain related to knee OA and was found superior to viscosupplementation.**
 13. Narouze SN. Ultrasound-guided cervical spine injections: ultrasound "prevents" whereas contrast fluoroscopy "detects" intravascular injections. *Reg Anesth Pain Med.* 2012;37(2):127–30.
 14. Hashemi M, Aryani MR, Momenzadeh S, et al. Comparison of transforaminal and parasagittal epidural steroid injections in patients with radicular low back pain. *Anesth Pain Med.* 2015;5(5), e26652.
 15. Chou R, Hashimoto R, Friedly J. Epidural corticosteroid injections for radiculopathy and spinal stenosis: a systematic review and meta-analysis. *Ann Intern Med.* 2015;163(5):373–81. **The benefit of Epidural steroid injections which are commonly performed in outpatient settings was concluded to be small and transient in this meta-analysis. This has ignited a debate in the field of Pain Medicine about an established treatment modality.**
 16. Chou R, Hashimoto R, Friedly J, et al. Pain management injection therapies for low back pain. technology assessment report ESIB0813. Rockville, MD: Agency for Healthcare Research and Quality; 2015. <https://www.cms.gov/medicare/coverage/determinationprocess/downloads/id98ta.pdf>.
 17. Cohen S. Epidural Steroid Injections: commentary on Chou et al *Ann Int Med* 2015. ASRA newsletter. 2015 Nov. 13-14. **Discusses shortcomings of Chou et al study and questions the Agency of Healthcare research and Quality's recommendations based on this study.**
 18. Kaye A, Manchikanti L, Abdi S, et al. Efficacy of epidural injections in managing chronic spinal pain: a best evidence synthesis. *Pain Physician.* 2015;18:E939–E1004.
 19. Smith DI, Hawson A, Correll L. Transversus abdominis plane block and treatment of viscerosomatic abdominal pain. *Reg Anesth Pain Med.* 2015;40(6):731–2.
 20. Barua JM, Arance I, Angulo JC et al. A systematic review and meta-analysis on the efficacy of intravesical therapy for bladder pain syndrome/interstitial cystitis. *Int Urogynecol J.* 2015; doi:10.1007/s00192-015-2890-7
 21. Pelletier F, Girardin M, Humbert P et al. Long-term assessment of effectiveness and quality of life of onabotulinumtoxinA injections in provoked vestibulodynia. *J Eur Acad Dermatol Venereol.* 2015; doi: 10.1111/jdv.13437.
 22. Ilfeld BM, Meunier MJ, Macario A. Ambulatory continuous peripheral nerve blocks and the perioperative surgical home. *Anesthesiology.* 2015;123(6):1224–6. **Randomized, controlled trial that provided evidence for non inferior outcomes and early hospital discharge with use of ambulatory continuous nerve blocks in orthopedic surgery.**
 23. Kenes MT, Leonard MC, Bauer SR, et al. Liposomal bupivacaine versus continuous infusion bupivacaine via an elastomeric pump for the treatment of postoperative pain. *Am J Health Syst Pharm.* 2015;72(23 Supplement 3):S127–32.
 24. Clarke H, Page GM, McCartney CJ, et al. Pregabalin reduces postoperative opioid consumption and pain for 1 week after hospital discharge, but does not affect function at 6 weeks or 3 months after total hip arthroplasty. *Br J Anaesth.* 2015;115(6):903–11.
 25. Souzdanitski D, Rech GR, Naydinskiy A. et al. Ketamine in perioperative analgesia for knee surgeries: review of evidence from randomized controlled trials. *Tech Reg Anesth Pain Manag.* 2015; doi:10.1053/j.trap.2015.10.012
 26. CDC: Injury Prevention and Control: Prescription drug overdose. <http://www.cdc.gov/drugoverdose/>. Accessed 30 Nov 2015
 27. Gasior M, Bond M, Malamut R. Routes of abuse of prescription opioid analgesics: a review and assessment of the potential impact of abuse-deterrent formulations. *Postgrad Med.* 2015 (just-accepted). **Provides a review of various FDA approved abuse deterrent opioid formulations. Use of these drugs might help to combat the problem of opioid abuse in certain situations.**
 28. Li Z1, Pergolizzi JV, Huttner RP et al. Management of opioid-induced constipation in pregnancy: a concise review with emphasis on the PAMORAs. *J Clin Pharm Ther.* 2015; doi: 10.1111/jcpt.12331.
 29. Rogríquez D, Urrutia G, Escobar Y, et al. Efficacy and safety of oral or nasal fentanyl for treatment of breakthrough pain in cancer patients: a systematic review. *J Pain Palliat Care Pharmacother.* 2015;29(3):228–46.
 30. Giusti A, Bianchi G. Treatment of complex regional pain syndrome type I with bisphosphonates. *RMD Open.* 2015;1 Suppl 1, e000056.
 31. Haanpää M, Cruccu G, Nurmikko T et al. Capsaicin 8% patch versus oral pregabalin in patients with peripheral neuropathic pain. *Eur J Pain.* 2015;. doi:10.1002/ejp.731
 32. Mercadante S. Topical amitriptyline and ketamine for the treatment of neuropathic pain. *Expert Review of Neurotherapeutics.* 2015;15(11):1249–53.
 33. Lynch ME. Cannabinoids in the management of chronic pain: a front line clinical perspective. *J Basic Clin Physiol Pharmacol.* 2015; doi:10.1515/jbcpp-2015-0059
 34. Zhang C, Xie Y, Luo X et al. Effects of therapeutic ultrasound on pain, physical functions and safety outcomes in patients with knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil.* 2015.

35. Cherian J, Harrison P, Benjamin S ET AL. Do the effects of transcutaneous electrical nerve stimulation on knee osteoarthritis pain and function last? *J Knee Surg.* 2015; doi:[10.1055/s-0035-1566735](https://doi.org/10.1055/s-0035-1566735)
36. Best TM, Moore B, Jarit P, et al. Sustained acoustic medicine: Wearable, long duration ultrasonic therapy for the treatment of tendinopathy. *Phys sportsmed.* 2015;43(4):366–74.
37. Koo CC, Lin RS, Wang T, et al. Novel noxipoint therapy versus conventional physical therapy for chronic neck and shoulder pain: multicentre randomised controlled trials. *Sci Rep.* 2015;5:16342. doi:[10.1038/srep16342](https://doi.org/10.1038/srep16342). **Noxipoint therapy or use of site - specific electrotherapy is being evaluated in comparison to standard PT. It is a promising new therapy.**
38. Gundmi AM. Effect of low level laser therapy on pain and quality of life in diabetic peripheral neuropathy. *Physiotherapy.* 2015;101:e495–6.
39. Zeidan F, Emerson NM, Farris SR. Mindfulness Meditation-Based Pain Relief Employs Different Neural Mechanisms Than Placebo and Sham Mindfulness Meditation-Induced Analgesia. *J Neurosci.* 2015;35(46):15307–25. **The authors used functional MRI in addition to standard parameters to demonstrate activation of supra spinal pain modulatory sites with Mindfulness Meditation.**
40. Schmidt S, Gmeiner S, Schultz C, et al. Mindfulness-based stress reduction (MBSR) as treatment for chronic back pain—an observational study with assessment of thalamocortical dysrhythmia. *Forsch Komplementmed.* 2015;22(5):298–303.
41. Twiddy H, Lane N, Chawla R, et al. The development and delivery of a female chronic pelvic pain management programme: a specialised interdisciplinary approach. *Br J Pain.* 2015;9(4):233–40.
42. Parkitny L, Wand BM, Graham C. interdisciplinary management of complex regional pain syndrome of the face. *Phys Ther.* 2015; Nov 19. [Epub ahead of print]
43. Cheung C, Park J, Wyman JF. Effects of yoga on symptoms, physical function, and psychosocial outcomes in adults with osteoarthritis: a focused review. *Am J Phys Med Rehabil.* 2015; Oct 22. [Epub ahead of print]
44. Chen B, Zhan H, Chung M et al. Chinese herbal bath therapy for the treatment of knee osteoarthritis: meta-analysis of randomized controlled trials. *J Evid Based Complementary Altern Med.* 2015; doi:[10.1155/2015/949172](https://doi.org/10.1155/2015/949172)
45. Hull A, Holliday SB, Eickhoff C, et al. The integrative health and wellness program: development and use of a complementary and alternative medicine clinic for veterans. *Altern Ther Health Med.* 2015;21(6):12–21.
46. Parker M, Delahunty B, Heberlein N et al. Interactive gaming consoles reduced pain during acute minor burn rehabilitation: a randomized, pilot trial. *Burns.* 2015; doi:[10.1016/j.burns.2015.06.022](https://doi.org/10.1016/j.burns.2015.06.022)
47. Blödt S, Pach D, Roll S, et al. Effectiveness of app-based relaxation for patients with chronic low back pain (Relaxback) and chronic neck pain (Relaxneck): study protocol for two randomized pragmatic trials. *Trials.* 2014;15:490.
48. Kazberouk A, Mcguire K, Landon BE. A survey of innovative reimbursement models in spine care. *Spine.* 2015; 1. doi:[10.1097/brs.0000000000001212](https://doi.org/10.1097/brs.0000000000001212). **The authors surveyed health care systems, physician groups and related institutions about their perspectives on newer payment models. It provides an insight into challenges faced by healthcare systems in the current socioeconomic climate.**
49. Katz J, Smith S, Collins J et al. Cost-effectiveness of nonsteroidal anti-inflammatory drugs and opioids in the treatment of knee osteoarthritis in older patients with multiple comorbidities. *Osteoarthritis Cartilage.* 2015; doi:[10.1016/j.joca.2015.10.006](https://doi.org/10.1016/j.joca.2015.10.006)