CHRONIC PAIN PERSPECTIVES™

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Diagnosing fibromyalgia and myofascial pain syndrome: A guide

PLUS

- A blueprint to managing multiple chronic conditions and pain
- How to safely prescribe long-acting opioids

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FEATURE ARTICLES

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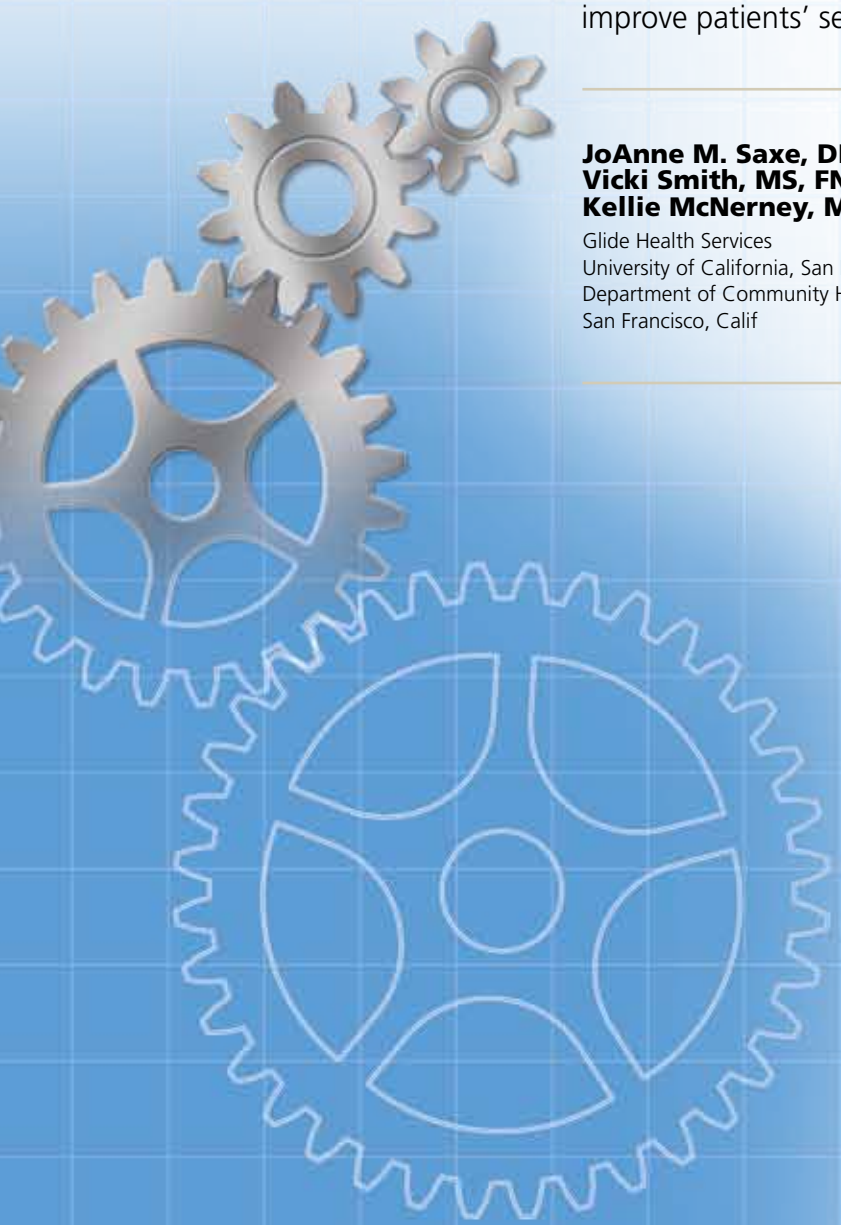
A blueprint to managing multiple chronic conditions and pain

Integrating medical and behavioral health services can improve patients' self-management skills and quality of life.



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Mr. S, age 64, receives care intermittently at a primary care health center for low-income individuals. His chronic conditions include hyperglycemia, hypertension, dyslipidemia, coronary artery disease (CAD), depression, and substance abuse. He also has chronic low back pain with associated radiculopathy. Chest pain related to his CAD and neuropathic pain in his right lower leg have worsened in the past year. He reports his pain as 8 out of 10, decreasing to 5 with opioid medication. His score of 20 on the Patient Health Questionnaire (PHQ-9) depression screen indicates severe depression.

His medications include methadone, gabapentin, low-dose aspirin, metformin, isosorbide dinitrate ER, metoprolol XR, lisinopril, atorvastatin, and docusate. He also uses acetaminophen with codeine for breakthrough pain. He reports greater than 95% adherence to this regimen.

When confronted about a positive urine

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The authors reported no potential conflict of interest relevant to this article.

Illustration: John J. DeNapoli

toxicology test, Mr. S admits to occasional use of "small amounts" of cocaine. A former cigarette smoker, he says he drinks 3 glasses of wine or smokes marijuana at night "to help me sleep." At his last clinic visit, he told his provider he didn't feel he needed substance abuse or mental health treatment.

Helping patients manage

Helping patients like Mr. S manage the signs, symptoms, and functional impairment of multiple chronic conditions (MCC) can seem overwhelming in a typical office visit. Issues related to chronic pain and substance abuse can further complicate care and worsen health outcomes.[1]

Objective criteria such as blood pressure readings or glucose tests are useful tools to diagnose medical conditions, whereas for chronic pain we must rely largely on patient reporting. Having only subjective data to support claims of chronic pain, a clinician may doubt a patient's truthfulness and miss opportunities to provide adequate care.

Furthermore, primary care providers now have legal mandates to coordinate care within their health homes and across affiliated clinical agencies and to measure outcomes.[2] Whatever the size of a practice, family physicians (FPs) and other primary care providers need to adopt best practices to address the complexities of MCC and chronic pain.[3]

An integrated health care model that includes behavioral health and substance abuse services can help address these imperatives. The advantage of this model is that patients may receive multiple services at one site, often in a single clinic visit, and from a team of collaborative providers. Compared with traditional models of care, this holistic approach to MCC can reduce duplication of services, cut costs, and improve patient outcomes.

So how does this approach work? To answer that, this article describes a patient-centered, integrated care model for the assessment and management of MCC, especially when accompanied by chronic pain and substance abuse. Our goal is to provide an evidence-based approach and specific interventions that you can apply in community practice.

Chronic illness: Common and often complicated

Chronic illnesses are conditions that last a year or more and require ongoing medical care and/or limit a person's activities of daily living.[4] MCC means having 2 or more concurrent chronic conditions. They may be:

- physical (eg, hypertension, CAD, diabetes, cancer, arthritis, chronic hepatitis, chronic renal insufficiency, chronic obstructive pulmonary disease, or asthma), or
- mental and cognitive disorders (such as depression, substance use disorders, or dementia).[4]

One in 4 US adults has MCC, including 21% with 2 or 3 chronic conditions and 4.9% with 4 or more.[5] The prevalence of MCC increases over the life span, such that as many as 3 in 4 adults age 65 and older have MCC.[5] The treatment of older adults with MCC accounts for 66% of the total US health care budget, according to the Department of Health and Human Services.[4]

The most common MCC combinations are the arthritis/hypertension dyad and the arthritis/diabetes/hypertension triad.[5] In older adults, cardiovascular disease, metabolic disorders, and pain disorders are the most common comorbidities, often occurring in tandem with anxiety/depression/somatoform disorders or neuropsychiatric disorders.[6,7] MCC often impairs physical, mental, and social health, with marked infringement on basic and instrumental activities of daily living.[3,8]

As many as 3 in 4 adults age 65 and older have multiple chronic conditions.

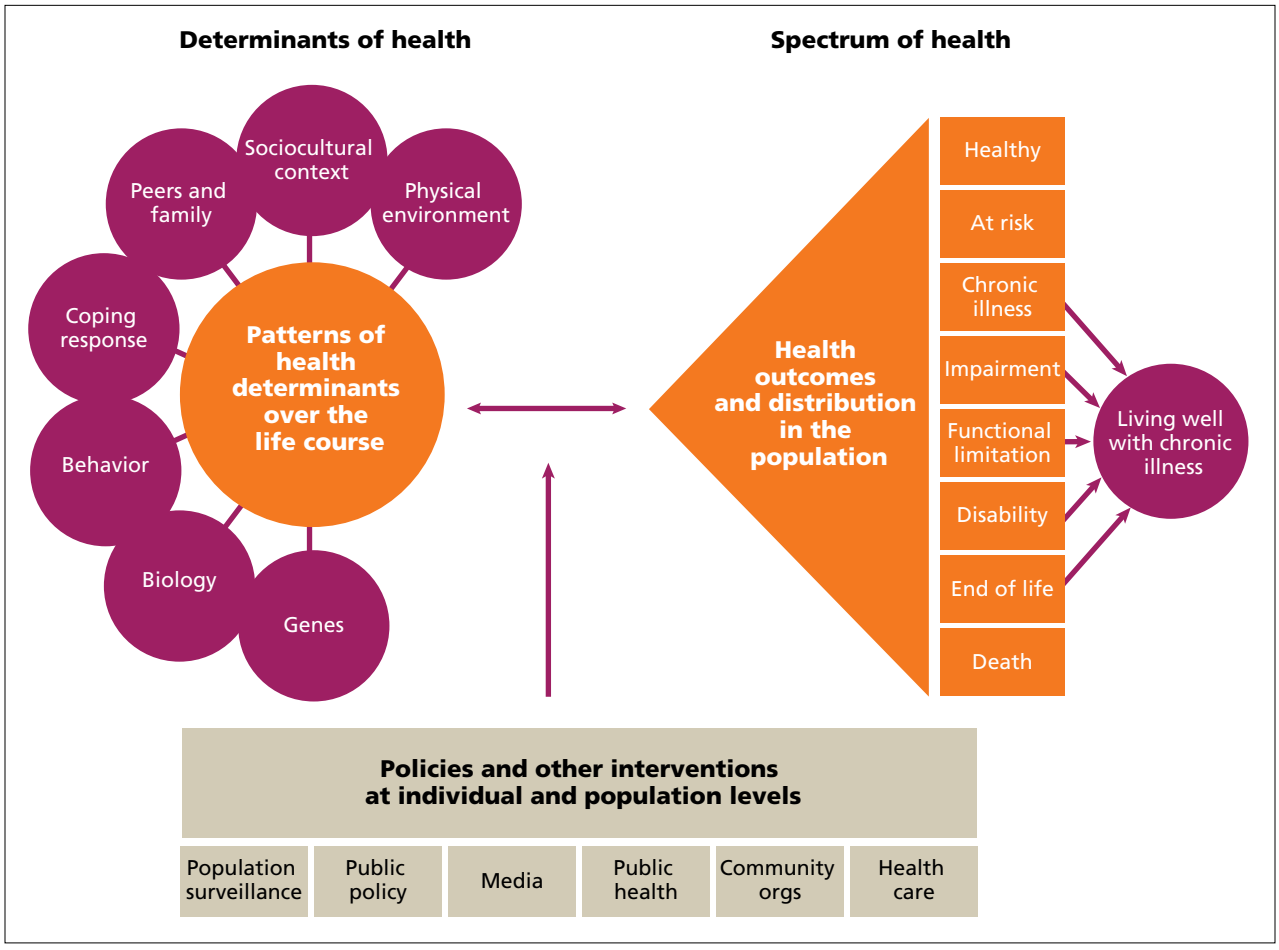
MCC and chronic pain: An integrated care delivery approach

People with chronic pain as a component of MCC report multiple physical signs and symptoms (eg, pain, fatigue, and depressed mood), cognitive deficits, functional impairments, and socioeconomic challenges. They suffer greater disability, poorer health, and diminished quality of life, compared with individuals with fewer symptoms and comorbidities.[9-13] Their challenges can become barriers that prevent them from receiving the comprehensive, multimodal treatment needed for effective symptom management.[2]

A clinician who understands these challenges and the lived experience of pain and MCC is best equipped to engage a patient in self-management of multiple chronic symptoms. Two evidence-based models can help build that understanding and assist with MCC-related assessments and management:

- The *Integrated Framework for Living Well with Chronic Illness*, from the Institute of Medicine,[13] emphasizes the importance of factors that determine a person's health (FIGURE 1). Genes, biology, behavior,

FIGURE 1: Integrated framework for living well with chronic illness



Source: Institute of Medicine. *Living Well with Chronic Illness: A Call for Public Health Action*. Washington, DC: The National Academies Press; 2012.[13] Reprinted with permission. Copyright 2012, National Academy of Sciences.

coping response, peers and family, sociocultural factors, and the environment all influence an individual's lifetime symptom experience and illness-wellness trajectory. These determinants also affect caregivers, the community, and society. Screening tools and other resources (TABLE 1) can help the clinician to understand the patient's health challenges and find opportunities for improvement.

- The *Chronic Care Model*[14] is a collaborative approach to chronic disease management developed by researchers from the Improving Chronic Illness Care initiative at the MacColl Institute for Healthcare Innovation. This model has been shown to enhance interactions between health care teams and patients and to improve outcomes.[15,16]

Clinicians who have integrated these 2 models report well-coordinated, continuous care for patients with complex health problems.[10,16] A number of Safety Net Clinics, including Glide Health Services (where we work), have adopted the core concepts of these models in their approach to the care of patients with MCC and chronic pain. (Glide Health Services is a nurse-managed clinic supported by the Glide Foundation, Dignity Health, and the University of California San Francisco School of Nursing.)

To support an integrated model of care, fundamental structural elements are needed to promote care coordination and effective communication among clinicians, staff, and affiliated community agencies. The Glide Health Services' integrated model of care for patients with MCC and chronic pain is based on the Chronic Care Model's 6 interventions to improve communication (TABLE 2):

- a culture of caring and improvement
- well-informed care partners with excellent teamwork skills
- electronic medical records (EMR) to track data and trends
- information to support clinical decision making

TABLE 1
Patient has multiple chronic conditions and pain? Consider these screening tools and other online resources

Condition, symptoms and/or functional status	Tools with online access	Description
Alcohol and other drugs screening	CAGE-AID http://www.cqaimh.org/pdf/tool_cageaid.pdf	4-item screening test for drugs and alcohol; 1 to 2 positive answers warrant further assessment
Depression screening	Patient Health Questionnaire (PHQ-9) http://www.integration.samhsa.gov/images/res/PHQ%20-%20Questions.pdf	9-item screening test with one item related to functional impact of depression
Pain assessment	Pain assessment tools in low resource settings http://www.iasp-pain.org/AM/Template.cfm?Section=Home&Template=/CM/ContentDisplay.cfm&ContentID=12173	Variety of assessment tools for children, adolescents, and adults
	PEG Scale: Pain that interferes with Enjoyment of life and General activity http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2686775/	3-item pain intensity and assessment scale
Assessment of personal health domains	PROMIS Computer Adaptive http://www.nihpromis.org/Patients/Measures	Test scales: anger, anxiety, depression, fatigue, pain behavior, pain interference, physical function, satisfaction with discretionary social activities and social roles
	World Health Organization Quality of Life-BREF (WHOQOL-BREF) http://www.who.int/substance_abuse/research_tools/whoqolbref/en/	26 items that measure physical health, psychological health, social relationships, and environment
Tobacco screening and brief intervention	Agency for Healthcare Research and Quality: Five major steps to intervention http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html	"5 As" (Ask, Advise, Assess, Assist, and Arrange)
Trauma screening	Primary Care PTSD Screen (PC-PTSD) http://www.ptsd.va.gov/professional/pages/assessments/pc-ptsd.asp	4-item screening test related to traumatic experiences; any positive answer warrants further assessment
Clinical management guidelines	Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain http://www.jpain.org/article/S1526-5900(08)00831-6/fulltext	Systematic review by the American Pain Society and American Academy of Pain Medicine

- support groups to encourage patient self-management
- community advocacy for individuals with chronic pain.[14,16]

All of these elements warrant attention when designing coordinated care for individuals with chronic conditions. Primary care clinicians who lack the resources to provide comprehensive services for patients affected by MCC and chronic pain could collaborate with community providers, agencies, and volunteers to expand health and wellness options.

At Glide Health Services, for example, the Chronic Pain Team has engaged volunteer services—including an acupuncturist, a tai chi instructor, and a diabetes educator—to help meet patients' care needs. Additional strategies and tools are available to guide primary care providers in implementing and evaluating an integrated approach to MCC (TABLE 3).

Intervention #1:
A culture of caring and improvement

An integrated model of care hinges on an engaged leadership team that supports clinicians, staff, and community affiliates as they work to bring together primary care and

TABLE 2
Chronic Care Model: 6 interventions to improve communication

Organization of health care

1. Culture of caring
2. Delivery system design
3. Information systems
4. Decision support
5. Self-management support

Community

6. Resources and policies

↓

Lead to productive interactions between patients and providers

↓

Result in improved health outcomes

Source: Improving Chronic Illness Care. The Chronic Care Model.[14] Available at: http://www.improvingchroniccare.org/index.php?p=The_Chronic_Care_Model&s=2.

Important elements of an integrated model of care include a certified substance abuse treatment program, HIV counseling and testing, and case management services.

behavioral health services. Important elements of this model include a certified substance abuse treatment program, HIV counseling and testing, and wellness and case management services.

A continuous quality improvement program ensures that clinical practices are evidence-based, efficient, and serve the patient population. For example, a multiprofessional chronic pain committee at Glide Health Services:

- develops policy and procedures
- reviews and embeds chronic pain guidelines in the EMR
- addresses management and performance of patient groups with similar demographics and/or health conditions
- reviews and approves self-management programs and material, and
- discusses patient scenarios at monthly meetings to address care-related concerns.

Intervention #2:
Well-informed care partners with excellent teamwork skills

Staff, clinicians, and community partners who are well informed in MCC and chronic nonmalignant pain are essential to an integrated approach for patients with substance use disorders, mental health disorders, and psychosocial barriers.

- Clinic team members may include behaviorists, complementary care providers, clerks, medical assistants, nurse practitioners, pharmacists, physicians, registered nurses, and social workers.
- Community team members may include clerics, exercise trainers, home care aides, physical and/or occupational therapists, and/or physician specialists.

Roles and responsibilities should be clearly defined. Communication and teamwork skills need to promote productive provider-to-patient interactions and patient self-management.[17] Regular communications, such as daily team huddles to discuss emerging patient concerns, and monthly case reviews and Web-based referrals and consultations can help to meet the above goals.

Intervention #3:
EMRs to track data and trends

When caring for individuals with chronic pain and MCC, systems to ensure seamless access to care and consistent follow-up are imperative. The health care team and organizational structure also need to be evaluated. EMRs provide tools to build chronic pain registries to track individuals and measure standard performance indicators (such as access to care, no-show rates, symptom management, functional status, and satisfaction of care).

Intervention #4:
Information to support clinical decision making

The care team needs evidence-based guidelines for assessing and managing MCC and chronic pain, as well as validated, culturally appropriate patient education materials. Ideally, these resources will be embedded in the EMR for ready access during clinical visits.

The Glide Health Services' pain treatment services include pain treatment agreements (FIGURE 2) and periodic urine toxicology screening. The primary care providers screen for histories of trauma and violence, depression, and substance and tobacco use (TABLE 1) at the initial visit and then quarterly (or more frequently, if indicated).[16] Based on results, primary care clinicians often refer individuals to a behavioral health clinician for evaluation. The primary care provider can make additional

TABLE 3
Toolkits for coordinating care in a primary care practice

Resource and Web access	Description
Improving Chronic Illness Care Available at: http://www.improvingchroniccare.org/index.php?p=Care_Coordination&s=326	Site for the Chronic Care Model. Describes how primary care practitioners can set up teams with other care providers. Toolkits: • present case reports that illustrate what care coordination means and why achieving it is both important and challenging • introduce a care coordination model and key concepts for successful referrals and care transitions • discuss 6 changes that support the model and resources to make those changes • provide an index of recommended tools and resources.
TeamSTEPPS Primary Care Available at: http://www.ahrq.gov/professionals/education/curriculum-tools/teamstepps/primarycare/	The Agency for Healthcare Research and Quality has developed a useful guide to help office-based clinicians organize an effective teamwork system. The original TeamSTEPPS program was designed to improve patient safety and communication skills among health care professionals. TeamSTEPPS Primary Care adapts the core concepts of the original program to reflect the environment of primary care office-based teams. It offers handouts, slide presentations, and instructional videos.

recommendations for the patient's pain treatment agreement.

Intervention #5:
Support groups for patient self-management

Encouraging self-care is also important. To encourage nonmedication treatment and self-care, Glide Health Services' providers offer additional support structures.

- *Chronic pain support groups* use a workbook that guides patients through pain-related issues. Central to this is moving patients from a singular focus on pain and medication discussions to behavioral changes that may enhance their life experiences.
- A *Pain Management Plus Group* focuses on alcohol, tobacco, and drug education in the context of opioid medications. Its goals are to help individuals avoid pain agreement violations and overdose, and to explore alternatives to substance use for coping with dysphoric moods and life stressors.

Intervention #6:
Community advocacy for individuals with chronic pain

Helping patients with MCC requires that caregivers advocate for them on the community level. To this end, Glide Health Services' nurse practitioners participate on a citywide chronic pain committee with members from San Francisco Safety-Net Clinics. This interprofessional committee develops and disseminates evidenced-based, compassionate guidelines to help individuals affected by chronic pain to safely use opioid medications, as indicated, and to lead functional, productive lives. Together, committee members are building a list of community agencies that provide patient resources (such as low-cost fitness programs) that no agency alone can offer. These advocacy efforts promote consistency with community standards and best practices.

How effective is this model? We'll find out

In 2012, the Glide Health Services' Chronic Pain Team began a comprehensive chart analysis of 127 patients with chronic pain to assess the effectiveness of this integrated care model. All of the patients have MCC and one or more mental health diagnoses, most commonly depression or post-traumatic stress disorder. All are considered at high risk for substance abuse, with approximately 60% having a history of it. The study is to be completed in 2014.

FIGURE 2: Glide Health Services pain treatment agreement

Client Information
Name:
DOB:
MR#
Date:

The purpose of this agreement is to prevent misunderstandings about certain medicines you will be taking for pain management or other medical conditions. This agreement will help both you and your provider comply with laws and clinic policies regarding controlled pharmaceuticals.

I, _____ and _____ have decided together

Client Name *Provider Name*

to use a controlled substance for management of pain or another medical condition.

MEDICATION	INSTRUCTIONS	AMOUNT PER WEEK/MONTH

I agree that this medication will only be used by myself and as it is prescribed.

I will not share, sell or trade my medication with anyone.

I will safeguard my medication from loss or theft. Lost or stolen medicine will not be replaced.

If I run out of the medication, Glide Health Clinic will not refill the prescription early.

I will not seek controlled substances from other medical providers.

I understand that there will be no refills on my medications without a provider visit at Glide.

I understand that my medication will not be refilled at a drop-in visit.

I agree to share my complete medications history in order to avoid adverse drug interactions.

I will attend all my scheduled appointments, including any referral appointments my clinician has made for me, and follow up as designated in my plan of care.

I agree to bring all unused pain medication to every office visit.

I understand pharmacy records may be reviewed to confirm prescriptions.

I understand I may be required to have random urine or blood testing completed. I agree to this testing, and understand that if I fail to do so, I will be safely tapered off the medication(s).

I understand that I may be required to attend non-medication groups and/or therapies, and that failure to do so may result in termination from the pain treatment program (list agreed to activities/therapies).

I understand if I break this agreement, my provider may stop prescribing these pain medicines.

I understand that many pain medicines may cause drowsiness, impair my ability to drive and operate machinery, and may impair my thinking and judgment.

I understand that misuse of these drugs or use of these drugs in combination with alcohol, unauthorized prescription medications, or illicit drugs may have serious effects including death.

The prescribing provider has explained that the above medications have possible side effects and may be addictive.

Comments:

_____ _____

Client's Signature *Date*

_____ _____

Provider Signature *Date*

Source: McNerney K, Saxe JM, Pfeifer K. Chronic nonmalignant pain management. In: Collins-Bride GM, Saxe JM, eds. *Clinical Guidelines for Advanced Practice Nursing: An Interdisciplinary Approach.* 2nd ed. Burlington, MA: Jones & Bartlett Learning; 2013:423-436.[16]

CASE: Mr. S makes progress

When Mr. S enrolled in the Glide Health Services chronic nonmalignant pain program, he frequently attended acupuncture and the chronic pain support group. He also had a one-time trial of physical therapy. He received depression and substance use/tobacco screening (PHQ-9 survey and CAGE-AID) every 3 months, and annual urine toxicology screening per the program protocol.

Mr. S was referred to a psychiatrist for an updated evaluation and, as a result, was started on disulfiram. He agreed to abstain from alcohol and cocaine. He attended an opioid safety-training meeting and a "Pain Management Plus" group. He also agreed to weekly clinic visits for one month, alternating between mental health and primary care to support his revised treatment plan. Thereafter, Mr. S had primary and mental health care visits every other week until his EMR documented adherence to his plan of care.

Via the EMR and during monthly meetings, the chronic pain provider team—an internist, nurse practitioners, pharmacist, psychiatrist, and social worker—discussed and agreed on Mr. S's care plan and progress. Mr. S himself proposed an additional monthly urine toxicology test at his cardiologist's lab to "prove" his commitment to sobriety so that he might be considered for coronary artery bypass graft surgery.

Mr. S continues to be alcohol and drug free, with improved mood and sleep. He receives ongoing care and support through the Glide Health Services patient-centered, team-based, and integrated behavioral approach to care.

References

1. Peppin JF. The marginalization of chronic pain patients on chronic opioid therapy. *Pain Physician*. 2009;12:493-498.
2. Public Law 111-148, 111th Congress. The Patient Protection and Affordable Care Act. March 23, 2010. HR 3590. Congressional Record. Available at: http://www.gpo.gov/fdsys/pkg/PLAW-111publ148/pdf/PLAW-111publ148.pdf. Accessed October 31, 2013.
3. Parekh AK, Goodman RA, Gordon C, Koh HK; HHS Interagency Workgroup on Multiple Chronic Conditions. Managing multiple chronic conditions: a strategic framework for improving health outcome and quality of life. *Public Health Rep*. 2011;126:460-471.
4. US Department of Health and Human Services. *Multiple Chronic Conditions—A Strategic Framework: Optimum Health and Quality of Life for Individuals with Multiple Chronic Conditions*. Washington, DC: US Dept of Health and Human Services; 2010. Available at: http://www.hhs.gov/ash/initiatives/mcc/mcc_framework.pdf. Accessed October 25, 2013.
5. Ward BW, Schiller JS. Prevalence of multiple chronic conditions among US adults: estimates from the National Health Interview Survey, 2010. *Prev Chronic Dis*. 2013. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3652717/. Accessed October 25, 2013.
6. van den Bussche H, Koller D, Kolonko T, et al. Which chronic diseases and disease combinations are specific to multimorbidity in the elderly? Results of a claims data based cross-sectional study in Germany. *BMC Public Health*. 2011;11:101. Available at: http://www.biomedcentral.com/1471-2458/11/101. Accessed October 25, 2013.
7. Schäfer I, von Leitner EC, Schön, G, et al. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One*. 2010;5:e15941. doi:10.1371/journal.pone.0015941.
8. National Institutes of Health. PROMIS®: Dynamic tools to measure health outcomes from the patient perspective. Available at: http://www.nihpromis.org/default#2. Accessed October 31, 2013.
9. Brooks PM. The burden of musculoskeletal disease—a global perspective. *Clin Rheumatol*. 2006;25:778-781.
10. Butchart A, Kerr EA, Heisler M, et al. Experience and management of chronic pain among patients with other complex chronic conditions. *Clin J Pain*. 2009;25:293-298.
11. Elliott AM, Smith BH, Penny KI, et al. The epidemiology of chronic pain in the community. *Lancet*. 1999;354:1248-1252.
12. Kerns RD, Otis J, Rosenberg R, Reid MC. Veterans' reports of pain and associations with ratings of health, health-risk behaviors, affective distress, and use of the healthcare system. *J Rehabil Res Dev*. 2003;40:371-379.
13. Institute of Medicine. *Living Well with Chronic Illness: A Call for Public Health Action*. Washington, DC: The National Academies Press; 2012. Available at: http://www.iom.edu/Reports/2012/Living-Well-with-Chronic-Illness.aspx. Accessed October 26, 2013.
14. Improving Chronic Illness Care. The Chronic Care Model. Available at: http://www.improvingchroniccare.org/index.php?p=The_Chronic_Care_Model&s=2. Accessed October 25, 2013.
15. Coleman K, Austin BT, Brach C, Wagner EH. Evidence on the Chronic Care Model in the new millennium. *Health Aff*. 2009;28:75-85. Available at: http://content.healthaffairs.org/content/28/1/75.full.html. Accessed October 25, 2013.
16. McNerney K, Saxe JM, Pfeifer K. Chronic nonmalignant pain management. In: Collins-Bride GM, Saxe JM, eds. *Clinical Guidelines for Advanced Practice Nursing: An Interdisciplinary Approach*. 2nd ed. Burlington, MA: Jones & Bartlett Learning; 2013:423-436.
17. Agency for Healthcare Research and Quality. TeamSTEPPS® primary care version. Available at: http://www.ahrq.gov/professionals/education/curriculum-tools/teamstepps/primarycare/. Accessed October 25, 2013.

We have begun a comprehensive chart analysis to assess the effectiveness of the integrated care model. Results are expected next year.

How to safely prescribe long-acting opioids

By watching for certain pitfalls and tapping into FDA initiatives that include the REMS program, you can reduce the likelihood of opioid abuse and misuse.

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Illustration: John J. DeNapoli

Although opioids have been used for thousands of years to manage pain, the modern era has seen several impressive advances in their synthesis, formulation, and usefulness. Despite these advances, however, opioids continue to pose a risk for many patients. Even a cursory look at the data from emergency department (ED) visits highlights those risks.

Statistics from the Drug Abuse Warning Network indicate that among 4.9 million drug-related ED visits in 2010, 1.3 million were for misuse or abuse of pharmaceuticals; 425,247 of these visits involved narcotic pain relievers.[1]

To reduce the number of ED visits and deaths that result from opioid misuse and abuse, the Food and Drug Administration (FDA) decided in April 2011 to add extended-release opioids, long-acting opioids, and methadone to its risk evaluation and mitigation strategies (REMS) program to ensure appropriate prescribing practices. (See "The ABCs of REMS," on page S13).

Disclosure
The author reported no potential conflict of interest relevant to this article.

Availing oneself of opioid REMS programs is just one of the many ways to minimize the risk to patients who are being prescribed opioids. Staying abreast of the literature on the subject is, of course, another. To that end, I've put together the following overview geared toward family physicians. In the pages that follow, I review the mechanism of action of long-acting opioids, discuss possible adverse effects and drug tolerance, and explain how to adhere to the FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.[2]

Understanding the mechanism of action

Opioids work at multiple receptors within the central and peripheral nervous systems, including the mu, kappa, and delta receptors. Each opioid has its own unique binding affinity for each receptor. The analgesic effects and the adverse effects from opioid therapy both arise from the drug's interaction with the receptors. The primary mechanism of action is the alteration of the perception of pain through the mu opioid receptor. This presynaptic inhibition is responsible for decreasing the release of excitatory neurotransmitters, such as substance P and glutamate.

Opioids are indicated for patients with the moderate to severe pain that accompanies various diseases. In September 2013, however, the FDA announced class-wide labeling changes for extended-release and long-acting opioids. Labels will now state that these formulations are indicated for the management of pain "severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate."

Opioid analgesics can be divided into 3 broad categories:

Pure agonist opioids include morphine, oxycodone, fentanyl, hydromorphone, and oxymorphone, to name a few. The analgesic or adverse effects of these agents do not reach a ceiling, which means when the dose increases, there is generally an increase in the analgesic activity and potential for adverse effects.

Partial agonists include buprenorphine, butorphanol, and nalbuphine. These drugs do have a ceiling effect to their analgesic efficacy; continuous dose increases will not lead to an increase in analgesic effect. However, the potential for opioid adverse effects can increase as the dose increases for these agents. Partial agonists also have an effect on pure agonist opioids in that partial agonists can actually decrease their full analgesic effect. So if, for example, a patient taking oxycodone around the clock is given a dose of buprenorphine, he or she may go into acute opioid withdrawal because of the addition of the partial agonist, which can displace the pure agonist on the mu receptor.

Antagonists include naloxone and methylnaltrexone. These agents are pure opioid antagonists and are used to reverse the adverse effects of opioids. Reversal of the opioid adverse effects in general also reverses their pain-mediating effects. There are some exceptions to this, but that topic is outside of the scope of this review.[3]

Some opioids have activity on other receptors, as well as on opioid receptors. These include tapentadol, which is an agonist of the mu opioid receptor and a norepinephrine reuptake inhibitor, and methadone, which is an opioid agonist and an *N*-methyl-D-aspartate (NMDA) receptor antagonist.

Be prepared for adverse reactions

Adverse effects of opioids include sedation, psychomotor slowing, hyperalgesia, constipation, immune suppression, pruritus, and hormonal imbalance. These drugs can, for instance, cause decreases in testosterone, estrogen, and cortisol blood concentrations.[4] Opioids also have a direct effect on the medulla, suppressing cough and decreasing respiratory drive. Respiratory depression is a real concern, especially for patients who are not tolerant to the

THE ABCs OF REMS

The concept of risk evaluation and mitigation strategies (REMS) programs was introduced in 2007 by the Food and Drug Administration (FDA) as a way to educate not only health care professionals but also patients regarding the safe and effective use of certain prescription medications. Medications that are subject to REMS are more likely to cause harm—through appropriate or inappropriate use—and undergo more stringent postmarketing analysis by the FDA.

The first opioid REMS program, produced by Boston University School of Medicine, was launched online on March 1, 2013. (See https://search.er-la-opioidrems.com/Guest/GuestPageExternal.aspx for details.) Similar programs have followed throughout the country. Although physicians are not required by law to participate in REMS, the FDA encourages all opioid prescribers to voluntarily participate. Accredited continuing education (CE) activities of opioid REMS programs are supported by independent educational grants from manufacturers of extended-release and long-acting opioids.

The FDA's goal is to have more than half of long-acting opioid prescribers educated by 2017.

A REMS program is just one of the many ways to minimize the risk to patients who are being prescribed opioids.

effects of opioids. In addition, patients with certain conditions are already at increased risk for respiratory depression, such as those with chronic obstructive pulmonary disease, obesity, or recent abdominal surgery.

Respiratory depression can progress to respiratory arrest and death. Two key ways to reduce the risk for respiratory depression are to (1) start opioid therapy at a low dose and titrate upward slowly and (2) take into account incomplete cross-tolerance between individual opioids when switching the patient from one opioid drug to another (opioid rotation). And, of course, combining an opioid with another respiratory depressant, such as alcohol, benzodiazepines, or barbiturates, greatly enhances the risk of respiratory depression, hastening its onset and increasing the possibility of respiratory arrest or death. Such combinations should be avoided.

Like other opioids, methadone can cause respiratory depression, but there are also unique issues to be mindful of with this medication. Although its low cost makes it attractive to a physician who is concerned about the patient's budget, the pharmacokinetics of methadone are widely variable, with a half-life ranging from 8 to 59 hours.[5] Due to this wide variation in half-life, dosing changes with methadone should therefore be done with no greater frequency than 5 to 7 days from the last upward titration to prevent adverse effects.

Drug interactions between methadone and several other medications can cause QTc interval prolongation that can progress to lethal heart arrhythmias. Thus, patients who are taking other medications that can increase the QTc interval—including amiodarone, citalopram, and flecainide, antibiotics such as clarithromycin, azithromycin, and moxifloxacin, and antiretroviral medications—should have periodic electrocardiographic monitoring. A complete list of medications that can increase the QTc interval is available elsewhere.[6]

Patients who are taking methadone and other medications that can increase the QTc interval should have periodic ECG monitoring.

Opioid tolerance

Patients who are tolerant to opioids are appropriate candidates for extended-release opioids, long-acting opioids, or transmucosal immediate-release fentanyl (TIRF) formulations. Opioid tolerance[7,8] is defined by the FDA as the following doses for more than 7 days:

- morphine ≥ 60 mg per day orally
- oxycodone ≥ 30 mg per day orally
- fentanyl transdermal ≥ 25 µg/h
- oxymorphone ≥ 25 mg per day orally
- hydromorphone ≥ 8 mg per day orally
- any other opioid agent at an equianalgesic dosing schedule

TABLE
Which extended-release and long-acting opioid medications are subject to REMS?

Generic name	Brand name(s)
Buprenorphine transdermal system	Butrans
Fentanyl transdermal system	Duragesic
Hydromorphone ER	Exalgo
Morphine CR, ER, SR	Avinza Kadian MS Contin Oramorph
Oxycodone CR	OxyContin
Oxymorphone ER	Opana ER
Transmucosal immediate-release fentanyl (TIRF) formulations	
Fentanyl buccal soluble film	Onsolis
Fentanyl citrate buccal tablet	Fentora
Fentanyl citrate oral transmucosal lozenge	Actiq
Fentanyl nasal spray	Lazanda
Fentanyl sublingual tablet	Abstral

CR, controlled release; ER, extended release; REMS, risk evaluation and mitigation strategy; SR, sustained release.

Sources: http://www.er-la-opioidrems.com/IwgUI/rems/products.action; http://www.tirfremsaccess.com/TirfUI/rems/pdf/education-and-ka.pdf.

The FDA is requesting manufacturers to incorporate this information into the package inserts and REMS programs for extended-release and long-acting opioids.

You will need to monitor patients for opioid tolerance, which can occur after a patient has been on a particular dose of opioid for an extended time. Analgesic tolerance should be weighed in the context of the patient's overall functionality to determine if a dose increase is appropriate or if the opioid therapy should be modified to provide better functional capacity.

How does REMS fit in?

Currently, only extended-release and long-acting opioids and TIRF products are subject to a REMS (TABLE). (We will use the term REMS opioids to distinguish these opioids from non-REMS opioids, which are more commonly prescribed and are not currently subject to REMS.)

Opioids outside of the current REMS program include immediate-release oral opioids (tablets, capsules, solutions, and suspensions), opioid/nonopioid combination products (including hydrocodone/acetaminophen and oxycodone/ibuprofen), and parenterally administered opioids (such as morphine IV and hydromorphone IM). The primary rationale behind this delineation between "REMS opioids" and "non-REMS opioids" lies in the amount of opioid in a single dose unit. Many of the extended-release and long-acting opioids and the rapid-onset opioids have a total amount of opioid that, if abused, could lead to significant opioid adverse effects, including respiratory depression.[9]

Consider, for example, a patient taking 6 10-mg tablets of immediate-release oxycodone in 24 hours vs a patient taking 60 mg of long-acting oxycodone in 24 hours. A patient who is opioid naive could experience both the analgesic and adverse effects from either formulation. However, extended-release or long-acting opioids contain large amounts of pure opioid agonist or partial agonist compared with immediate-release opioids. If these formulations are altered—for instance, if they are crushed, punctured, or the extended-release technology is otherwise disrupted—a "dose dump" can occur that turns that extended-release opioid into an immediate-release opioid. Even patients who are tolerant to opioids can experience severe adverse effects from this, including respiratory depression and death.

As mentioned, TIRF formulations are also subject to REMS. These products contain high concentrations of fentanyl, a potent synthetic opioid appropriate for patients who are tolerant to conventional dosing of immediate-release and extended-release or long-acting opioids. Each TIRF formulation releases fentanyl differently, and each manufacturer explicitly states that the formulations are not interchangeable, even for microgram-equivalent doses. A patient who is not tolerant to opioids and uses the product as directed can experience severe adverse effects, including respiratory depression and death.[10]

For REMS Web resources, see the box on page S17.

Adhering to the FDA Blueprint

As part of the opioid REMS program, manufacturers of extended-release and long-acting opioids must provide (1) education for prescribers of these medications through grant-funded accredited continuing education (CE) activities and (2) information that prescribers can use when counseling patients about the risks and benefits of these opioid analgesics. The FDA Blueprint outlines the following 5 broad topics the agency believes are crucial for practitioners to understand when they prescribe REMS opioids[2]:

Patient assessment. This should include, at a minimum, weighing benefits against risks, including the potential for abuse, misuse, or diversion by the patient or the patient's contacts. Your assessment should also include a complete history, including family and social history, especially if it concerns substance abuse, a complete physical examination, and appropriate documentation. The American Academy of Family Physicians has published an executive summary on pain management and opioid abuse that complements many aspects of this article.[11]

Several opioid risk assessment tools are available to help stratify patients with low, medium, or high risk for abuse or misuse of opioids. These tools should be used at regular intervals, not just on the initial patient interview to begin REMS opioid therapy. Some of the more commonly accepted tools in the literature include:

- ORT (Opioid Risk Tool), available at: http://www.partnersagainstpain.com/printouts/Opioid_Risk_Tool.pdf
- DIRE (Diagnosis, Intractability, Risk, Efficacy), available at: http://www.opioidrisk.com/node/1202
- SOAPP-R (Screener and Opioid Assessment

Crushing or puncturing an opioid can lead to a "dose dump" in which an extended-release formulation becomes one that is an immediate release.

for Patients with Pain-Revised), available at: www.painedu.org/soapp.asp

- SISAP (Screening Instrument for Substance Abuse Potential), available at: http://www.stoppain.org/pcd/_pdf/OpioidChapter9.pdf

If REMS opioid therapy is appropriate for your patients, it's helpful to identify specialists in addiction and psychiatric disease for referral for those who are at higher risk of opioid misuse or abuse. While this is not a requirement of the opioid REMS, it is highly recommended from a documentation standpoint. Many communities do not have direct access to specialists, and their consultation may not be practical for the patient; however, for highest-risk patients, utilizing a specialist and documenting these referrals protects not only the patient, but also the physician prescribing the REMS opioid.

Initiation, modification, and discontinuation of treatment. Start patients who are appropriate candidates for a REMS opioid on the lowest dose of the medication to prevent acute opioid overdosing. Also be mindful of the proper dose titration for each agent, and assess for safety and efficacy with each titration.

Use the extended-release or long-acting opioid as the background or baseline amount of opioid for that patient and use immediate-release opioids, nonopioid analgesics, and nonpharmacologic strategies to supplement the long-acting and extended-release opioid. Adult patients with breakthrough cancer pain who are tolerant to around-the-clock opioids are appropriate candidates for TIRF formulations.

Also note that when converting from one opioid to another, the equianalgesic conversion charts available in the literature are not an end-all-be-all when calculating a dose. Most of the data used to create these charts were unidirectional studies in patients with acute pain.

To account for possible incomplete cross-tolerance between opioids, 25% to 50% reductions in opioid conversion dose may be warranted to prevent overdosing the opioid and thus reduce the risk of adverse effects, including respiratory depression. For example, for patients who are satisfied with their pain control on an opioid but are experiencing adverse effects, reduce the total dose by 50% when calculating the equianalgesic dose of the new opioid. Another example: If a patient is experiencing adverse effects and his or her pain control is not ideal, consider a reduction of 25% of the equianalgesic dose of the opioid.

But in some cases, no reduction in equianalgesic opioid dosage is called for when one takes into account incomplete opioid cross-tolerance. Such would be the case when a patient does not experience enough pain relief with his or her current opioid to allow for activities of daily living. Rotating to another opioid may help determine if opioid analgesic therapy would still be appropriate to ease this patient's suffering.

Managing patients who continue with treatment. In some respects, you will want to treat patients who have pain the way you would treat patients with high blood pressure, high cholesterol, or diabetes; set goals at the outset of the diagnosis and discuss them with the patient. Focus these goals on expectations for both the patient and the clinician regarding quality of life, activities of daily living, and functional improvement. Evaluate these goals with appropriate frequency to ensure safe and effective use of the REMS opioids.

How often you evaluate the treatment regimen depends on the formulation of the opioid; however, in general, an appropriate initial opioid trial would be approximately 7 days to assess for safety and efficacy. During periodic reassessments, reinforce the importance of adhering to dosing strategies, ensuring that patients are aware that misuse and abuse could happen at any time, by the patient or by his or her friends and family.

Just as the status of a patient's hypertension or diabetes changes over time, so too will his or her pain.

Just as the status of a patient's hypertension or diabetes changes over time, so too will his or her pain. For example, you modify antihypertensive medication regimens after assessing the patient's progress, or lack thereof. Similarly with opioid medications, if the patient shows improvement, taper the medication down to prevent adverse effects. If a particular opioid is not working, you may need to increase the dose or rotate to another opioid to better manage the patient's pain.

Urine drug tests. One strategy worth considering is the appropriate use of urine drug tests to ensure that the patient is taking the opioid as prescribed. Such testing can also determine that no illicit or nonprescribed medications or substances are present in the patient's urine. Also use opioid drug screens to satisfy the requirement for documentation, should your charts be audited. Proper documentation, accompanied by urine screening, can help establish that a clinician is following best practices.

Keep in mind that opioid drug tests have their limitations. Not all opioids will show up on screening tests; qualitative tests are needed to detect certain synthetic opioids, including oxycodone and methadone. Also remember that

because many opioids have metabolites, testing positive for the parent compound and not the metabolite may indicate misuse or abuse because the patient is not taking the prescribed opioid often enough for the metabolite to show up on the screening.

Also consider the use of an opioid treatment agreement as part of your documentation. This protects both the prescriber and the patient, outlining topics such as monitoring frequency, early refills, urine drug testing, and patient discharge from the practice.

Patient counseling. It's important that you ensure that patients understand the safe use, storage, and disposal of their medication. Educating patients on the benefits, risks, and proper use of extended-release and long-acting opioids is essential. Many of the counseling points for REMS opioids are located on the FDA's Web site, www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm. Some of these points are also included in the medication guide for patients (a guide in plain language that is given to the patient when the medication is dispensed from the pharmacy). This guide should be reviewed with the patient while he or she is on a REMS opioid.

Here are some of the counseling points to discuss before initiating or continuing a REMS opioid:

1. Remind patients that they should take medication only in the dose and frequency prescribed, and to discuss any changes from this schedule with their physician before making those changes.
2. Discuss all medications the patient is currently taking, including those prescribed by other providers, over-the-counter medications, and complementary and alternative medicines.
3. Instruct patients to keep all opioid medications away from other people, including children and pets. These medications should also be protected from theft by locking them away when the patient is not taking his or her dose.
4. Explain that these REMS opioids are intended for patients with a tolerance to other opioid medications and they are not to be shared with other individuals. Also warn them not to alter the dose formulation by splitting or crushing or otherwise attempting to extract the opioid from the intended dose; this could lead to significant adverse events, including death.
5. Inform patients of the adverse effects of opioid therapy, highlighting respiratory depression as a serious and possibly fatal event. Respiratory depression generally occurs in patients who are acutely exposed to higher doses of opioids. For patients who are tolerant to opioids, the likelihood of respiratory depression is decreased; however, all changes in opioid dosage, especially increases, may raise the risk of respiratory depression in the short term.
6. Tell patients to inform their physician about any adverse effects they experience. Prescribers may contact the FDA as needed regarding recurrent common or unique drug adverse effects.

Most, if not all, patients who use opioids will experience constipation. In many cases, dietary fiber and appropriate hydration may help ameliorate the problem. Also consider mild stimulant laxatives (such as senna) or some bulk-forming agents (such as polyethylene glycol) to prevent constipation. A stimulant or bulk-forming agent is generally required for continued use to prevent constipation. On the other hand, a softener/surfactant such as docusate, used alone, will not help counteract the decreased gastrointestinal peristalsis that opioids cause.

Also discuss drug interactions with your patients. Central nervous system (CNS) depressant medications can increase the risk of sedation and somnolence, especially if combined with alcohol. Stress the importance of not consuming alcohol with opioids, as this can lead to severe CNS and respiratory depression. All opioids—and methadone in particular—need to be carefully scrutinized by a physician if a patient is using any other CNS depressant medications, including benzodiazepines and barbiturates. Emphasize that respiratory depression can occur during the initiation or dose-escalation phase.

REMS WEB RESOURCES

- **Approved risk evaluation and mitigation strategies (REMS)**
  www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm
- **The extended-release and long-acting opioid analgesics risk evaluation and mitigation strategy**
  www.er-la-opioidrems.com/IwgUI/rems/home.action
- **Transmucosal immediate release fentanyl (TIRF) products risk evaluation and mitigation strategy (REMS): Education program for prescribers and pharmacists**
  www.tirfremsaccess.com/TirfUI/rems/pdf/education-and-ka.pdf

When a patient tests positive for a parent compound and not the metabolite, it may indicate misuse or abuse.

Product-specific drug information. When counseling patients, be sure to cover other pertinent issues that are medication specific. For instance, explain to patients who are taking long-acting or extended-release preparations (oxycodone extended release, morphine extended release, hydromorphone extended release), that they should swallow extended-release pills whole and not alter the medication (tablets or capsule), because doing so could lead to respiratory depression or death.

If the patient is using a fentanyl patch, it is important to not alter the patch or place a heat source (electric heating pads, for instance) over the application site. Doing so could also increase the risk of respiratory depression or death.

References

1. Center for Behavioral Statistics and Quality, Substance Abuse and Mental Halth Services Administration. The DAWN report: highlights of the 2010 Drug Abuse Warning Network (DAWN) findings on drug-related emergency department visits. July 2, 2012. www.samhsa.gov/data/2k12/DAWN096/SR096EDHighlights2010.htm. Accessed November 12, 2013.
2. US Food and Drug Administration. FDA blueprint for prescriber education for extended-release and long-acting opioid analgesics. July 9, 2012. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed November 12, 2013.
3. Yuan CS. Methylnaltrexone mechanisms of action and effects on opioid bowel dysfunction and other opioid adverse effects. *Ann Pharmacother*. 2007;41:984-993.
4. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician*. 2008;11(2 suppl):S105-S120.
5. National Library of Medicine. Methadone (methadone hydrochloride) injection. DailyMed Web site. dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=5581#nlm34090-1. Accessed November 12, 2013.
6. Drugs that prolong the QT interval and/or induce torsades de pointes. CredibleMeds Web Site. http://www.crediblemeds.org/everyone/composite-list-all-qtdrugs/?rf=US. Accessed November 12, 2013.
7. Transmucosal Immediate-Release Fentanyl (TIRF) REMS Industry Group (TRIG). Transmucosal immediate release fentanyl (TIRF) products risk evaluation and mitigation strategy (REMS): Education program for prescribers and pharmacists. TIRF REMS Access Program Web site. www.tirfremsaccess.com/TirfUI/rems/pdf/education-and-ka.pdf. Accessed November 12, 2012.
8. REMS Program Committee (RPC). The extended-release and long-acting opioid analgesics risk evaluation and mitigation strategy. ER/LA Opioid Analgesics REMS Web site. www.er-la-opioidrems.com/IwgUI/rems/home.action. Accessed November 12, 2013.
9. US Food and Drug Administration. Questions and answers: FDA approves a risk evaluation and mitigation strategy (REMS) for extended-release and long-acting (ER/LA) opioid analgesics. FDA Web site. www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm309742.htm. Accessed November 12, 2013.
10. US Food and Drug Administration. Transmucosal immediate-release fentanyl (TIRF) medicines. FDA Web site. www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm282110.htm. Accessed November 12, 2013.
11. American Academy of Family Physicians. Pain management and opioid abuse: a public health concern. Position paper. Executive summary. AAFP Web site. http://www.aafp.org/dam/AAFP/documents/patient_care/pain_management/OpioidAbusePositionPaperFINAL.pdf. Accessed November 12, 2013.

Diagnosing fibromyalgia and myofascial pain syndrome: A guide

The instruments and physical exam techniques described here will help you to diagnose these 2 common soft-tissue pain conditions.

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Fibromyalgia (FM) and myofascial pain syndrome (MPS) are common soft-tissue pain conditions seen in medical practice. These conditions have similar pathophysiologic processes, are associated with many of the same comorbidities, and can occur concomitantly.

The best estimate for the incidence of FM is 2% to 4% of any population, regardless of the country.[1] The incidence of MPS is more difficult to estimate. Most studies reporting on incidence or prevalence of these disorders start with a base population of patients who present with complaints of pain (generally) or musculoskeletal pain (specifically),[2,3] underscoring the need for timely recognition, diagnosis, and treatment of FM and MPS.

The approach to diagnosis has changed in recent years. The diagnosis of FM has been influenced by techniques using questionnaires for screening large populations. The role of

Illustration: Joe Gorman

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TABLE 1
Comorbid conditions found with fibromyalgia and myofascial pain syndrome*

Commonly associated with both FM and MPS	
Migraine headache	Pelvic pain syndrome
Tension-type headache	Vulvovaginitis
Temporomandibular joint disorder	Prostatitis
Fibromyalgia	Endometriosis
Hypermobility syndromes	Dysmenorrhea
Painful bladder syndrome	Hypothyroidism
Irritable bowel syndrome	
More commonly associated with MPS	
Vitamin D deficiency	
Vitamin B_{12} deficiency	
Iron deficiency	
Parasitic infection	
Celiac disease of malabsorption	

FM, fibromyalgia; MPS, myofascial pain syndrome.
*This list was developed based on the author's experience in treating patients with FM and MPS.

these questionnaires in clinical practice is still being examined.

The accuracy of MPS diagnosis had been questioned due to a paucity of studies substantiating the objectivity of physical findings. But a number of studies have now validated the physical examination of trigger points.

Imaging techniques using magnetic resonance imaging and ultrasound can demonstrate the physical features of the myofascial trigger point (MTrP). But their clinical utility is moot (as will be discussed below).

Similarities in pathophysiology of FM and MPS

Both FM and MPS are associated with *central sensitization*, an increased excitability of neurons in the dorsal horn of the spinal cord.

Fibromyalgia has been characterized as a central pain disorder arising from a dysfunctional pain modulation system. Nociceptive impulses reach the brain unimpeded by the usual action of the descending nociceptive inhibitory control system. However, there is also increasing evidence of a significant contribution from peripheral sources of pain such as the MTrP.[4-6] There is an increased incidence of fibromyalgia among first-degree relatives of individuals with fibromyalgia. Risk is also increased among certain populations with genetic polymorphisms affecting serotonergic and catacholaminergic systems.[7] Fibromyalgia can also occur after trauma, but this may be the result of widespread myofascial pain or the increase in central sensitization that can occur after trauma.

Fibromyalgia has 2 major components: chronic widespread pain and a set of somatic symptoms. Among FM patients, these components are expressed on a continuum, with one end of the spectrum being heavily weighted toward chronic widespread pain and the other end being largely a somatic symptom disorder.[1] FM's association with MPS occurs more often on the chronic pain side of the spectrum. The association of pain in FM with other comorbid conditions, such as migraine, painful bladder, and irritable bowel syndrome (TABLE 1), suggests a more widely systemic somatic disorder. However, other associated conditions, such as fatigue and abdominal symptoms, have become part of the new diagnostic paradigm for fibromyalgia.

MPS begins as a peripheral disorder in which pain originates within the muscle as the MTrP. It is uniquely characterized by localized tenderness and hardness in a discrete taut band within a muscle. (It is also the peripheral source of pain in fibromyalgia, mentioned earlier.)

When the MTrP has been present for some time—as little as days in some cases, and certainly within a few weeks—peripheral and central sensitization occur, leading to the development of *referred pain*.[8] The patient usually presents with a complaint related to referred pain. The diagnosis of MPS, therefore, requires an awareness that the cause of pain may lie at a distance from the site of pain.

Diagnosing FM: 2010 preliminary diagnostic criteria

The 2010 fibromyalgia diagnostic criteria[9,10] of the American College of Rheumatology (ACR) are applied in a 2-part, self-administered questionnaire. Part 1 assesses pain at 19 sites depicted on a body diagram or listed in a table. This part of the questionnaire is the Widespread Pain Index (WPI) (TABLE 2).[9] Part 2 of the questionnaire is the Symptom Severity (SS) scale, which measures the intensity of such symptoms as fatigue, headache, and abdomi-

nal pain (TABLE 3).[9] The patient scores each item as 0 (not present) to 3 (severe).

Changes from the 1990 ACR criteria. The previous ACR diagnostic criteria[11] established the extent of tenderness by palpation at 18 predetermined sites. Involvement of at least 11 of these sites indicated that tenderness existed in 3 quadrants of the body. If the patient's pain had lasted 3 months, clinicians could exclude transient pain and presume a diagnosis of FM.

The 1990 criteria were developed as a research tool to be used by trained clinicians in guaranteeing a uniform selection of subjects for studies. However, the criteria became widely used clinically and were even adopted by insurance carriers as the basis for reimbursement for treatment of fibromyalgia. Symptoms and comorbid conditions were not used in the diagnosis of fibromyalgia, although their association with fibromyalgia was widely understood.

In its 2010 modifications, the ACR eliminated palpation as a diagnostic criterion.

Scoring the modified ACR 2010 screening questionnaire

Clinicians have scored the modified ACR 2010 diagnostic criteria in one of 2 ways. Both approaches score the WPI and the SS scale separately and then add the results. One way confirms the presence of fibromyalgia if the WPI is ≥7 and the SS scale is ≥5.[10] The other way requires that a WPI score of 3-6 be accompanied by an SS scale score ≥9. A combined score of 12 has yielded specificity and sensitivity of more than 90%, but a score of ≥13 has shown a sensitivity of 96.6% and a specificity of 91.8% when compared with a clinical diagnosis made by experienced clinicians.[10]

Limitation of the modified ACR 2010 criteria

In abandoning the detection of tender points, the new ACR criteria have shifted thinking about FM away from its having a basis in peripheral pain elements that influence central nervous system pathways and moved it toward the perception of FM being a systemic somatic condition. The emphasis now is on a symptom complex, and that has had important implications for treatment.

Treatment now emphasizes cognitive-behavioral therapies to address depression and catastrophic thinking and kinesiophobia that alter the work, social, and family-related

TABLE 2[9]
Potentially painful locations on the Widespread Pain Index, modified ACR 2010 fibromyalgia diagnostic criteria

Bilateral sites (total of 14)	Unilateral sites (total of 5)
Jaw	Neck
Shoulder	Upper back
Upper arm	Chest/breast
Lower arm	Abdomen
Hips	Lower back
Upper leg	
Lower leg	

Scoring methods to confirm presence of fibromyalgia
Widespread Pain Index ≥7 and Symptom Severity scale score ≥5
OR
Widespread Pain Index of 3-6 and Symptom Severity scale score ≥9

Widespread Pain Index scoring: The patient identifies the presence of pain in any of the 19 areas specified. Score will be between 0 and 19.

ACR, American College of Rheumatology.

TABLE 3[9]
Symptom Severity scale items in the modified ACR 2010 fibromyalgia diagnostic criteria

Items related to fatigue, cognitive difficulties, and sleep disturbances	Items related to specific symptoms
Fatigue	Abdominal pain or cramps
Trouble thinking	Depression
Waking up tired	Headache
Items that are not scored but exclude transient illness and other conditions, such as cancer or lymphoma, which can produce similar symptoms	
Symptom duration of ≥3 months	
Patient does not have a disorder that would otherwise explain the pain	

Scoring methods to confirm presence of fibromyalgia
Widespread Pain Index ≥7 and Symptom Severity scale score ≥5
OR
Widespread Pain Index of 3-6 and Symptom Severity scale score ≥9

Symptom Severity scale scoring: The patient rates each item 0 (not present) to 3 (severe).

ACR, American College of Rheumatology.

TABLE 4
Diagnostic features of myofascial pain syndrome

Features that must be present to diagnose myofascial pain syndrome
Taut band within the muscle
Exquisite tenderness at a point on the taut band
Reproduction of the patient's pain by stimulating the taut band at the trigger point
Features helpful, but not required, for diagnosing myofascial pain syndrome
Local twitch response (important to elicit by needling when treating by injection or deep dry needling)
Referred pain (common and a cause of many myofascial pain syndromes)
Weakness
Restricted range of motion
Autonomic signs, eg, skin warmth or erythema, tearing, piloerection (goose-bumps)

Adapted from: Simons DC, Travell JC, Simons LS. *Myofascial Pain and Dysfunction: The Trigger Point Manual*. 2nd ed. Baltimore, Md: Lippincott Williams & Wilkins; 1999.

TABLE 5
Step-by-step procedure for identifying myofascial trigger points*

1. Take the patient's history and use a pain drawing to identify pain locations
a. The history identifies the areas affected by pain and suggests possible provocative and perpetuating factors.
b. The pain drawing shows where the patient experiences pain.
2. Conduct examination
a. Select a muscle whose trigger points can refer pain to an affected area.
b. Lay the nonpalpating hand gently on the patient at a nonpainful site away from the trigger point. This first touch is nonthreatening. The patient's movements are now controlled by the clinician.
c. Palpate the muscle for taut bands, using either flat palpation or pincer palpation.
d. Move the fingers along the taut band to find the trigger point—the hardest and most tender spot in the taut band.
3. Compress the trigger point manually
a. Ask the patient if the spot is tender or painful, and, if so,
b. Ask the patient if the elicited pain resembles his or her usual pain.
4. Compress the trigger point for 5 to 10 seconds and then ask if there is pain or some sensation away from the trigger point (referred pain).

*This is the protocol that is used at the author's clinic, Pain and Rehabilitation Medicine, in Bethesda, Md.

behavior of the patient. Coupled with a graduated exercise program, this approach has been highly successful in reducing the burden of dysfunction in FM patients.

Reconsidering the role of MTrP in fibromyalgia. Unfortunately, the de-emphasis of the physical examination for FM means that the MTrP, which has been shown to be clinically important,[4-6,12] may be overlooked in practice. Indeed, there has been a corresponding de-emphasis of treating tender points and a corresponding increase in using cognitive-behavioral and psychological therapies.

MTrPs are found at FM tender point sites, and referred pain from these trigger points corresponds closely to the patient's own pain. Inactivation of these trigger points has reduced fibromyalgia pain.[6] For patients who meet screening criteria for FM, clinicians should still perform a physical examination that evaluates for causes of widespread pain, including joint disease and MTrP.

Diagnosing MPS

MPS is a condition with a major peripheral component, the MTrP. As mentioned, the MTrP, even after a few days, induces central sensitization in which there is hypersensitivity (increased response to a painful stimulus) or allodynia (a painful response to a normally nonpainful stimulation). The result is that the patient has local tenderness and distant (referred) pain. Referred pain is the result of central sensitization in the spinal cord dorsal horn, and this explains many of the pain syndromes seen in the clinic. Further, referred pain mimics other pain syndromes that range from joint disease and radiculopathies to visceral pain.

The importance of manual examination

Manual examination of muscle to identify MTrP is the basis for diagnosing MPS. And it serves additional purposes (in FM as well, although it's no longer required in the ACR diagnostic criteria), because touch:

- is the beginning of establishing trust
- begins the healing process
- allows the examiner to evaluate range of motion, quality of joints, quality of the skin and underlying tissues, and organs such as the thyroid gland and tissues such as lymph nodes
- allows identification of trigger points as a source of tenderness

TABLE 6[21]
Laboratory tests commonly used in the evaluation of patients with myofascial pain syndrome

Condition	Symptoms	Tests	Threshold
Hypothyroidism	Diffuse muscle pain Widespread MTrPs Deep coldness Fatigue Constipation	TSH Serum cholesterol	TSH >2.25 µIU/mL
Iron insufficiency	Diffuse muscle pain Widespread MTrPs Fatigue Deep coldness	Serum ferritin Serum iron, IBC, percent transferrin saturation Hemoglobin, HCT, differential count	Ferritin <25 ng/mL Low serum iron, high IBC, transferrin saturation <18% HCT <28, MCH and MCHC low
Vitamin D insufficiency	Diffuse pain Widespread MTrPs Fatigue Weakness	25-OH vitamin D PTH if vitamin D is very low	25-OH vitamin D <30 ng/mL Test PTH if 25-OH vitamin D <18 ng/mL
Vitamin B_{12}	Diffuse pain Weakness Impaired vibration and position sense in the great toes	Vitamin B_{12} level CBC	Serum vitamin B_{12} level <350 pg/mL Macrocytic anemia
Parasitic infestation	Diffuse myalgia Widespread MTrPs Gastrointestinal symptoms	3 stools on different days for ova and parasites	Stool positive for ova and/or parasites
Candida infection	Recurrent vaginal itching and discharge Widespread pain Diffuse muscle tenderness	History of recurrent episodes of vaginal candidiasis History of repeated use of antibiotics	Vaginal exam may or may not be positive for *Candida*

CBC, complete blood count; HCT, hematocrit; IBC, iron-binding capacity; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MTrPs, myofacial trigger points; PTH, parathyroid hormone; TSH, thyroid-stimulating hormone.

- can activate the trigger point and elicit the referred pain patterns that account for the patient's pain.

Imaging may not prove clinically practical

The MTrP as an entity has been established by 2 imaging procedures: magnetic resonance elastography (MRE)[13,14] and ultrasonoelastography.[15-17] These imaging procedures are research tools and are not clinically useful at this time. Although there is some interest in guiding treatment by trigger point needling or injection using ultrasound, MTrP identification by manual palpation is rapid and has proven to be reliable between trained examiners.[18-20]

Trigger point features

The MTrP has a number of diagnostically relevant features. Foremost among these is the *taut band*.

The taut band is a discreet band of contracted muscle fibers within the belly of the muscle. The taut band contracts sharply when

stimulated. It is the first feature to appear in MPS and the last to go away. The taut band can be present when there is no pain. Trigger point pain is not present in the absence of a taut band.

The tender zone in an MTrP is always in the taut band and located in the hardest, most contracted portion of the band.

An *active* trigger point is spontaneously painful with activity or at rest. A *latent* trigger point is not spontaneously painful but is tender to palpation.

A *nontender taut band* is just called a taut band. It is the essential abnormality in the muscle; it is activated with muscle activity and can become latent or active. The *tender, taut band* is relevant when activation of it by palpation or by needling reproduces the pain a patient has experienced.

Essential trigger point features for diagnosis (TABLE 4). Three features are required to diagnose MPS:

- *taut band*
- *tender, hard area* on the taut band
- *reproduction of patient's pain* by stimulating the taut band at the trigger point.

Despite the recent de-emphasis of the physical exam in fibromyalgia, it's important to consider the potential role of trigger points.

A detailed, step-by-step diagnostic procedure for the identification of the trigger point (which we use in our clinic) is presented in TABLE 5. Commonly used laboratory tests useful in identifying conditions relevant to initiating or sustaining of MTrP syndromes appear in TABLE 6.[21]

Approach to treatment

Treatment of FM aims to restore the function of the descending nociceptive inhibitory system using selective norepinephrine reuptake inhibitors, gabapentinoids, and other drugs. Additional treatments include cognitive-behavioral therapy, gradually progressive physical therapy, restoring adequate sleep patterns, and treating comorbid medical conditions, such as hypothyroidism. (See "A common clinical scenario for chronic pain" below.) It's also useful to treat peripheral sources of pain, such as trigger points, associated with fibromyalgia.[6,22]

MPS may respond to medications such as analgesics or antidepressants. Physical therapy can also help, as can injections with or without (dry needling) lidocaine. Steroids and other sub-

A COMMON CLINICAL SCENARIO FOR CHRONIC PAIN

Ms. W, a 44-year-old woman, had experienced widespread pain, fatigue, and sleep disturbance for 10 years. She complained of memory difficulties and had trouble focusing on topics. Her work and home life suffered. She was always tired and ached constantly. She found no relief from multiple physical therapy sessions or treatments with serotonin-norepinephrine reuptake inhibitors or gabapentinoid drugs. She also described an uncontrollable urge to move her legs and sometimes her arms, which was worse at night. She had heavy menstrual periods and frequent episodes of loose stools or constipation.

Physical examination showed widespread tenderness in both shoulder girdle and pelvic/hip girdle regions bilaterally, as well as in the extremities. Tender taut bands were present in many muscles, with referred pain elicited from many of these sites.

Laboratory tests showed a vitamin D level of 18 ng/mL. The serum ferritin level was 20 ng/mL. Her hemogram showed red cells to be microcytic but she was not anemic. Thyroid function tests showed a thyroid-stimulating hormone level (TSH) of 3.16 µIU/mL, but the level 3 years earlier was 1.78 µIU/mL. Follow-up laboratory study showed her tissue transglutaminase antibody level to be elevated.

In addition to clear evidence of widespread myofascial pain syndrome, the patient's chronic widespread pain, sleep disturbance, fatigue, and cognitive dysfunction met the criteria for fibromyalgia. But she also had iron and vitamin D deficiencies, hypothyroidism, restless leg syndrome, and adult celiac disease with a malabsorption syndrome.

We started treatment with a gluten-free diet, iron and vitamin D replacement, and thyroid supplementation. Her restless leg syndrome diminished, resulting in better sleep. After 2 months, sleep had improved, fatigue was no longer a problem, energy levels increased, and cognitive function improved. Pain and muscle tenderness were lessened.

Comment: *This patient had widespread pain and trigger points secondary to malabsorption. Adult celiac disease is an autoimmune disorder commonly associated with other autoimmune disorders, such as hypothyroidism. The resulting malabsorption led to iron deficiency that, in turn, caused restless leg syndrome. She developed secondary widespread myofascial pain syndrome that met the criteria in this setting of fibromyalgia, according to the 1990 ACR criteria. We diagnosed this patient's condition not by questionnaire, but by physical examination, history, and laboratory testing. This is a common presentation in our clinic.*

stances such as vitamin B_{12} offer no advantage over lidocaine alone.

References

1. Wolfe F, Brähler E, Hinz A, Häuser W. Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. *Arthritis Care Res*. 2013;65:777-785.
2. Fernández-de-las-Peñas C, Gröbli C, Ortega-Santiago R, et al. Referred pain from myofascial trigger points in head, neck, shoulder, and arm muscles reproduces pain symptoms in blue-collar (manual) and white-collar (office) workers. *Clin J Pain*. 2012;28:511-518.
3. Kaergaard A, Andersen JH. Musculoskeletal disorders of the neck and shoulders in female sewing machine operators: prevalence, incidence, and prognosis. *Occup Environ Med*. 2000;57:528-534.
4. Ge HY, Wang Y, Fernández-de-Las-Peñas C, et al. Reproduction of overall spontaneous pain pattern by manual stimulation of active myofascial trigger points in fibromyalgia patients. *Arthritis Res Ther*. 2011;13:R48.
5. Alonso-Blanco C, Fernández-de-las-Peñas C, Morales-Cabezas M, et al. Multiple active myofascial trigger points reproduce the overall spontaneous pain pattern in women with fibromyalgia and are related to widespread mechanical hypersensitivity. *Clin J Pain*. 2011;27:405-413.
6. Affaitati G, Costantini R, Fabrizio A, et al. Effects of treatment of peripheral pain generators in fibromyalgia patients. *Eur J Pain*. 2011;15:61-69.
7. Buskila D, Neumann L. Genetics of fibromyalgia. *Curr Pain Headache Rep*. 2005;9:313-315.
8. Mense S, Gerwin R. *Muscle Pain: Understanding the Mechanisms.* Heidelberg, Germany: Springer-Verlag; 2010: Chapters 3-5.
9. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res*. 2010;62:600-610.
10. Ferrari R, Russell AS. A questionnaire using the modified 2010 American College of Rheumatology criteria for fibromyalgia: specificity and sensitivity in clinical practice. *J Rheumatol*. 2013;40:1590-1595.
11. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the Multicenter Criteria Committee. *Arthritis Rheum*. 1990;33:160-172.
12. Staud R, Robinson ME, Weyl EE, Price DD. Pain variability in fibromyalgia is related to activity and rest: role of peripheral tissue impulse input. *J Pain*. 2010;11:1376-1383.
13. Chen Q, Bensamoun S, Basford J, et al. Identification and quantification of myofascial taut bands with magnetic resonance elastography. *Arch Phys Med Rehabil*. 2007;88:1658-1661.
14. Chen Q, Basford J, An KN. Ability of magnetic resonance elastography to assess taut bands. *Clin Biomech*. 2008;23:623-629.
15. Sikdar S, Shah JP, Gilliams E, et al. Assessment of myofascial trigger points (MTrPs): a new application of ultrasound imaging and vibration sonoelastography. *Conf Proc IEEE Eng Med Biol Soc*. 2008;2008:5585-5588.
16. Turo, D, Otto P, Shah, JP, et al. Ultrasonic tissue characterization of the upper trapezius muscle in patients with myofascial pain syndrome. *Conf Proc IEEE Eng Med Biol Soc*. 2012;2012:4386-4389.
17. Sikdar S, Shah JP, Gebreab T, et al. Novel applications of ultrasound technology to visualize and characterize myofascial trigger points and surrounding soft tissue. *Arch Phys Med Rehabil*. 2009;90:1829-1838.
18. Gerwin RD, Shannon S, Hong CZ, et al. Interrater reliability in myofascial trigger point examination. *Pain*. 1997;69:65-73.
19. Sciotti VM, Mittak VL, DiMarco L, et al. Clinical precision of myofascial trigger point location in the trapezius muscle. *Pain*. 2001;93:259-266.
20. Bron C, Franssen J, Wensing M, Oostendorp RA. Interrater reliability of palpation of myofascial trigger points in three shoulder muscles. *J Man Manip Ther*. 2007;15:203-215.
21. Gerwin RD. A review of myofascial pain and fibromyalgia—factors that promote their persistence. *Acupunct Med*. 2005;23:121-134.
22. Staud R, Nagel S, Robinson ME, Price DD. Enhanced central pain processing of fibromyalgia patients is maintained by muscle afferent input: a randomized, double-blind, placebo-controlled study. *Pain*. 2009;145:96-104.