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The Daunting Challenge of Helping Millions of Patients Taper or Discontinue Opioid Therapy

The United States has made modest progress in reducing the unnecessary prescription of opioids for back and other forms of chronic pain in recent years. That in itself is a major achievement.

Generally speaking, the risk/benefit profile of long-term opioid use in most patients with chronic back pain is unfavorable. This is particularly true among individuals taking high doses—above those recommended by the 2018 Guideline from the Centers for Disease Control and Prevention. (See CDC, 2020.)

As a recent article in *JAMA Internal Medicine* by Roger Chou, MD, Anna Lembke, MD, and Jane Ballantyne, MD noted, "Evidence indicates that long-term opioid therapy confers little benefit versus nonopioid therapy, particularly for function." (See Chou et al., 2019.)

Or as Erin Krebs, MD, observed in the *Journal of General Internal Medicine*, "Overprescribing of opioid analgesics is understood to be a root cause of the ongoing US opioid overdose death and addiction crisis. For patients, overprescribing generates unnecessary exposure to risk of opioid-related injuries, opioid use disorder, and other adverse effects. Although the appropriate level of opioid prescribing is not always clear, examples of overprescribing are easy to find. For example, opioids are frequently prescribed for back pain even though they are not superior to other treatment options and not recommended in back pain management guidelines." (See Krebs, 2020.)

Another Intimidating Problem

However, the long-term over-prescription of opioids has left the United States with another intimidating problem.

There are millions of patients on long-term opioid therapy. Some of these individuals—a common estimate is two million—suffer from opioid use disorder (OUD) or addiction.

Others, however, fall short of satisfying the criteria for OUD. Instead they experience what has variably been named as complex persistent opioid dependence, refractory opioid dependence, or Opioid Dependence spelled with capital letters (OD).

The multiplicity of names is confusing. "It is a pity we haven't come to a consensus about what to call opioid dependence that isn't OUD [opioid overuse disorder or addiction]," said pain researcher Ballantyne, one of the pioneers in identifying this condition. "I favor 'complex persistent opioid dependence' because there is a good acronym. Acronyms matter. What's more, CPOD is the term we used when we first described refractory dependence in the first place." (See Ballantyne et al., 2012.)

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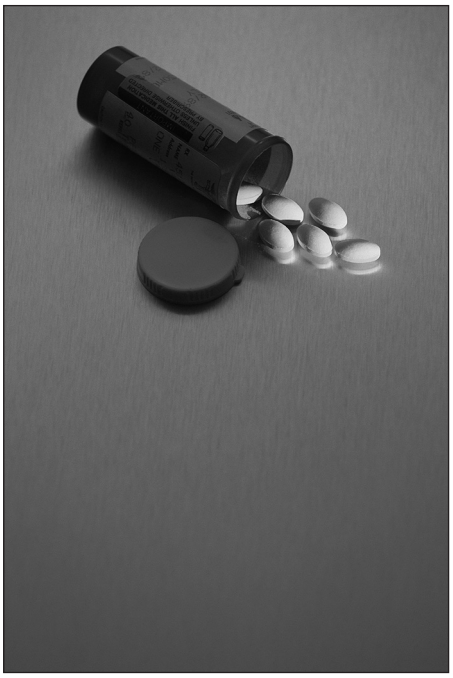

Mindless Back Care Costs

When people think about the exorbitant costs of spine care in the United States—currently estimated to be in excess of $85 billion per year—they usually focus on the many unnecessary diagnostic and treatment costs. They rarely think about the mindless and wasteful bureaucratic overheads that are pick-pocketing the American people.

A stunning new study found that healthcare administration costs in the United States accounted for more than a third of total medical spending—totaling more than $800 billion in 2017 alone. "The prices that US medical providers charge incorporate a hidden surcharge to cover their costly administrative burden," according to David Himmelstein, MD, and colleagues. (See Himmelstein et al., 2020.)

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Many Guilty Parties in the Opioid Crisis—Including the US Government

In parsing out blame for the opioid crisis, there are many "guilty" or "responsible" parties: opioid manufacturers, drug wholesalers, drug marketers, some pain societies, some pain specialists, some primary care doctors, to name a few.

However, US government agencies and their policies figure prominently on that list. This includes the FDA, which was asleep at the switch as the opioid crisis grew severe.

A study from Johns Hopkins University by James Heyward, MPH and colleagues recently pointed out that 50,000 individuals in the United States died from an opioid overdose in 2017. More than 2 million had a prescription opioid disorder. Forty percent of those deaths involved a prescription opioid.

About 60% of opioid volume in the United States in 2016 stemmed from extended-release/long-acting (ER/LA) opioids. And these accounted for an increased risk of abuse, addiction, overdose, and death.

The FDA Failed to Protect the Public

The FDA was aware of that and in 2012 mandated a "Risk Evaluation and Mitigation Strategy" (REMS) for these products.

"The REMS required ER/LA manufacturers to deliver voluntary REMS-adherent continuing education (CE) to prescribers, with content based on an FDA blueprint for safe ER/LA prescribing. Extended-release/long-acting opioid manufacturers were also required to develop medication guides to inform patients about risks associated with ER/LA opioids and to monitor and annually report on prescriber knowledge and behavior, as well as patient access and safety." (See Heyward et al., 2019.)

Unfortunately, because of inadequate study and monitoring of this program, the FDA was never able to determine whether it was useful and whether it did indeed reduce inappropriate prescribing, misuse, and abuse.

"Alternative observational study designs would have allowed for more rigorous estimates of the REMS effectiveness, improving the ability of the FDA and ER/LA manufacturers to critically evaluate and iteratively improve this important program," according to Heyward et al.

Another study from the same research group earlier this year found the FDA also failed to provide adequate oversight and monitoring of fentanyl products, which have killed tens of thousands of Americans. (See Rollman et al., 2019.)

"Both the FDA and the fentanyl makers failed to design and implement an effective monitoring program," said study senior author G. Caleb Alexander, MD, professor of epidemiology and medicine and co-director of the Center for Drug Safety and Effectiveness at the Johns Hopkins Bloomberg School of Public Health, in a report at the Johns Hopkins Medicine website.

So FDA policies and enforcement activities let the wrong people get the wrong drugs, to lethal effect.

Disclosures: None declared.

References:

Heyward J et al., Evaluation of the extended-release/long-acting opioid prescribing risk evaluation and mitigation strategy program by the US Food and Drug Administration: A review [published online ahead of print December 30, 2019], *JAMA Internal Medicine*; doi:10.1001/jamainternmed.2019.5459.

Rollman JE et al., Assessment of the FDA risk evaluation and mitigation strategy for transmucosal immediate-release fentanyl products, *JAMA*, 2019; 321(7): 676–85. doi:10.1001/jama.2019.0235.

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Beware of Paid "Patient Influencers" Promoting Controversial Treatments in Medicine and the Media

Drug and device companies have long relied on physicians and other healthcare providers to promote their products to the medical field and the general public. However, in recent years disclosure and transparency regulations have crimped some of the enthusiasm for being in the employ of corporate clients.

With the rise of social media some companies are branching out and employing large numbers of paid "patient influencers" to help market their products. And, unlike physicians, the patient influencers often do not disclose their financial ties.

A recent article at the *Health Affairs* blog by Judy Butler and Ariadne Fugh-Berman, MD, described a niche industry of companies that provide "patient influencers" for industry.

A Network of 100,000 Patient Influencers Across Medical Fields

Butler and Fugh-Berman offered the example of WEGO Health, a company representing over 100,000 patient influencers across medical fields.

This company is working hard to attract patient representatives. Here are some of the offers at the company website:

"Join the world's largest network of patient leaders and get paid for your insights and experience."

"Join the movement. Add your voice to our network. You have the story. You have the passion. Don't recreate the wheel when it comes to impacting the lives of others. Amplify your impact and become part of the WEGO Health Network."

"Get paid to share your story. You're not just a patient, you're the partner healthcare needs." (See WEGO, 2020.)

However, the recent article at the *Health Affairs Blog* suggests caution in interpreting the pronouncements of patient influencers—because their financial ties are often obscure.

"Most of WEGO Health customers are pharmaceutical companies, but they also cater to medical device manufacturers, hospitals, and insurers. Promoting what is known as disease awareness without naming a specific drug isn't regulated as advertising, so companies historically haven't had to reveal their involvement or funding. Even if patient leaders wanted to disclose payments, WEGO Health's terms of service include a comprehensive confidentiality clause that states that patients cannot disclose the identity of companies for whom they work," according to Butler and Fugh-Berman.

The Promotion of Opioids for Chronic Pain

In their article, the authors noted that patient influencers are particularly active in promoting the use of opioids for chronic pain.

Fugh-Berman described a patient influencer named Barby Ingle. "Ingle is the president of the International Pain Foundation, (iPain), a patient advocacy group for individuals with chronic pain. She has more than 18,000 followers on Twitter and defends the long-term use of opioids in chronic pain patients. On the iPain website, Ingle states, "The pain community and legislators need to ensure the patients in pain have appropriate access to care including opioid analgesics."

The researchers from Georgetown University pointed out that there is scant evidence supporting the effectiveness of daily long-term opioid use for most forms of chronic pain.

A 2019 article by Ingle at Pain Network News criticized a ruling by an Oklahoma judge that Johnson and Johnson contributed to the opioid crisis. The judge initially assessed a fine of $572 million in damages.

"Why force these pharmaceutical companies into settlements?" asked Ingle. "Why force an industry that saves millions of lives to do this? (See Ingle, 2019.)

"I don't believe that the pharmaceutical industry started, fueled, or conspired to create the largest public health crisis of our time. I don't believe there is an opioid epidemic. Addiction does affect millions of people but in many cases the help they need has not been provided. Billions of dollars in federal funding, including grants from President Trump's opioid initiatives, haven't been fully set up or spent to make a difference," Ingle argued.

Butler and Fugh-Berman criticized the article for a lack of financial transparency.

"Of course, everyone has the right to argue their point of view. But if that point of view is being bolstered and broadcast by a corporate entity with its own incentives and allegiances – that fact ought to be transparent. Nowhere in her articles about the opioid suit does Ingle disclose that she has recently received payments from Johnson & Johnson's subsidiaries and intermediaries like WEGO."

Several people, including Ingle and the founder of WEGO industries, have criticized the article by Butler and Fugh-Berman at the *Health Affairs Blog* website. In respect of "fair use" the *BackLetter* won't quote those letters or the response from Fugh-Berman. But they make fascinating reading and are available for free at the web address below.

Disclosures: None declared.

References:

Butler J and Fugh-Berman A, Patient influencers paid by pharmaceutical companies should be required to disclose industry ties, Health Affairs Blog, January 10, 2020; https://www.healthaffairs.org/do/10.1377/hblog20200109.985594/full/.

Ingle B, Johnson & Johnson verdict will harm chronic pain patients, Pain Network News, August 28, 2019; https://www.painnewsnetwork.org/stories/2019/8/28/johnson-amp-johnson-verdict-will-harm-chronic-pain-patients.

WEGO Health, Over 100,000 patient advocates and influencers working to transform healthcare; accessed January 21, 2020; https://www.wegohealth.com/.

Strong Opioids Rare After Spine Surgery in France

Opioid utilization after spine surgery depends heavily on overall opioid culture. Americans have come to believe that opioids are a necessary feature of post-surgical care. Yet in some other countries the prescription of strong opioids after spine surgery is a rarity.

A recent study from France illustrated these differences. However, the study design leaves some lingering questions.

Houssam Bouloussa, MD, has worked as a spine surgeon in both France and the United States. At the recent annual meeting of the North American Spine in Chicago, he described the differences in opioid culture, particularly in the postoperative setting, between the two countries.

In his presentation he discussed the liberalization of opioid utilization in the United States in the 1990s—a movement that has led to a major public health crisis. "It is probably the main reason that explains the decreased life expectancy of US residents over the last several years," he commented.

"Physician narcotic prescriptions have often been blamed for this crisis. I don't think we are the only culprits but maybe we don't want to take responsibility for it," he added.

No Opioid Crisis in France

Until recently, there was no major opioid crisis outside of North America, he observed. He noted that in France, where he used to work, there is still no significant opioid crisis. And strong opioids aren't used much, particularly for postoperative pain control. There appears to be less demand from patients. And there are fewer prescription for opioids after spine surgery, particularly for "smaller" cases, such as outpatient spine surgery.

"Opioids were rarely prescribed in France. Never for outpatient surgery—or rarely, in fewer than 5% of cases. And often not even after complex spine surgery," he explained.

Yet in the United States, opioids are prescribed almost universally after spine surgery.

Bouloussa and colleagues recently performed a study to compare the prescription of opioids following outpatient spinal decompression procedures in the United States and France. The operations included surgical procedures typically used for disc herniation (microdiscectomy) and spinal stenosis (unilateral laminotomy and unilateral laminotomy with bilateral decompression).

They studied pre- and postoperative opioid prescriptions among 50 patients in the United States and 50 in France. There were 31 males and nine females. The average age was approximately 41. There were eight surgeons in the French group and six in the American group.

Opioids were prescribed more frequently in the United States preoperatively and postoperatively. "A total of 25 American patients (50%) consumed narcotics preoperatively versus four French patients (8%)," according to Bouloussa and colleagues. Only 22% of the American patients were opioid-naive.

All of the American patients received an opioid prescription post-surgery. The most common drug was Percocet (hydrocodone/oxycodone plus acetaminophen). And they consumed a significant dose—a mean 617.04 mg morphine milligram equivalent.

NSAIDs and Tramadol

None of the French patients took strong opioids postoperatively. They relied mostly on nonsteroidal anti-inflammatory drugs.

However, there is a little hitch in this study. Thirty-one patients in the French also took a 50 mg daily dose of tramadol for up to 15 days. When tramadol was first developed, it wasn't regarded as an opioid. However, it clearly is, and it has some of the downside of opioids, including potential for dependence and addiction.

"Tramadol is a centrally acting analgesic with a multimode of action. It acts on serotonergic and noradrenergic nociception, while its metabolite O-desmethyltramadol acts on the μ-opioid receptor. Its analgesic potency is claimed to be about one tenth that of morphine," according to the World Health Organization. (See WHO, 2020.)

One American patient returned to an emergency department because of inadequate pain control. None of the French patients did.

So why are American consuming much higher levels of opioids following spinal decompression procedures? Bouloussa attributed this pattern to cultural differences.

He suggested that spine surgeons often prescribe opioids unnecessarily. "Cultural

beliefs among patients, physicians, and industry probably represent the most significant barrier against the implementation of a narcotic-free culture in our practices. Reducing narcotic prescriptions in our practices is not only feasible but also highly desirable," the study noted.

There are some obvious gaps and flaws in this study beyond the tramadol issue. It would have been useful to see data on post-surgical pain levels in the two groups—as well as overall surgical outcomes over both the short- and long-term.

However surgical groups all over the United States are working on ways to significantly reduce opioid consumption following spine surgery, including more invasive surgeries such as spinal fusion.

Some have suggested that the greater degree of bony disruption in major spine surgery leads to a greater need for opioids. This may prove true but needs to be studied more thoroughly.

And one hears case reports of fusion patients declining to take any opioids after surgery and still faring well with pain control. So the need for opioids likely varies from person to person. There is a tremendous need for further research to resolve these issues.

Disclosures: None declared.

References:

Bouloussa H et al., Differences between postoperative narcotic prescriptions in outpatient lumbar spine surgery between the United States and France, presented at the annual meeting of the North American Spine Society, Chicago, 2019; as yet unpublished.

WHO, Tramadol update review report, 2014; https://www.who.int/medicines/areas/quality_safety/6_1_Update.pdf.

Does Lifting With a Flexed Back Harm the Spine?

Numerous professional societies and government agencies have offered guidelines on safe lifting to protect the spine.

Physicians and other healthcare providers commonly repeat those recommendations to patients. They almost always include advice to "lift with the legs not the back." In other words, they tell patients and members of the public to avoid flexing the spine while lifting.

These recommendations always have two things in common: (1) They are offered with good intentions; and (2) They do not find much support in the scientific evidence. They often have a third feature in common: they usually do not acknowledge that they are based on consensus rather than definitive scientific evidence. *BackLetter* articles have emphasized these points repeatedly over the past 20 years.

Despite their lack of evidence support, many of these recommendations have slipped into standard clinical practice and governmental ergonomic policies. They have also led to population-wide beliefs that bending and lifting with a rounded back are dangerous to the spine.

A recent systematic review and meta-analysis from Curtin University in Australia is a reminder that much of the advice in this area is not "evidence-based."

Nic Saraceni, PT, and colleagues performed a review to determine whether lumbar spine flexion during lifting is a risk factor for the onset and/or persistence of low back pain. And to determine whether spinal flexion differentiates people with low back pain and those without. (See Saraceni et al., 2019.)

"Workplace health and safety representatives, healthcare practitioners, as well as gym instructors, advise that lifting with a rounded back should be avoided and instead insist that the safest way to lift is with a straight back," said senior author Peter O'Sullivan in a statement from Curtin University.

"We reviewed previous studies of participants who had lifted objects, ranging from a pen up to 12 kilograms in weight. We found no evidence to suggest that people who lift with a rounded back were at an increased risk of low back pain."

Disclosures: None declared.

Reference:

Saraceni N et al., To flex or not to flex? Is there a relationship between lumbar spine flexion during lifting and low back pain? A systematic review with meta-analysis [published online ahead of print November 28, 2019], *Journal of Orthopedic and Sports Physical Therapy*; doi:10.2519/jospt.2020.9218.

What Proportion of US Adults Have Back Pain?

A population-based US government report confirms that back pain is a common symptom in the United States affecting just under a third of adults over a three-month period.

The architects of the US National Health Interview Survey asked the simple question: "During the past three months, did you have lower back pain?" (See Centers for Disease Control and Prevention, 2020.)

Overall, 28% of men and 31.6% of women 18 years and older answered in the affirmative. Among men the prevalence of back pain rose gradually with age, up until the age of 74 years—when it began to decline.

Women reported higher levels of back pain than—by several percentage points—in the age groups 18 to 44, 45 to 64, and 75 years and older. Men and women reported similar levels of back pain in the 45- to 64-year age group.

It is hard to conclude much of anything based on the raw prevalence numbers in this survey. This survey did not differentiate between occasional aches and pains and more severe disabling symptoms. There were no attempts to categorize back pain by pain levels, chronicity, ability to function, or other criteria beyond age.

If would be useful if this survey asked about the prevalence of disabling back pain. Or back pain that led to medical care.

Disclosures: None declared.

Reference:

Centers for Disease Control and Prevention, *QuickStats*: Percentage of adults aged ≥18 years who had lower back pain in the past 3 months, by sex and age group—National Health Interview Survey, United States, 2018, *Morbidity and Mortality Weekly Report*, 2020; 68(5152):1196.

Erratum

BackLetter, 2020; 35(2):21

An article on page 21 of the February 2020 edition of the *BackLetter* addressed the role of antibiotics in the treatment of chronic back pain—in the presence of Modic changes. (See *BackLetter*, 2020.)

It inadvertently mischaracterized a study by Peter Fritzell, MD et al. with the statement "They studied the level of bacterial infection in two different groups: (1) forty adult patients with lumbar disc herniations and low back pain; and (2) twenty adolescents who underwent scoliosis surgery." (See Fritzell et al., 2019.)

As Fritzell kindly pointed out in a recent email, "In fact we did not, as we studied the *presence* of bacteria." This is an important distinction. The editors of the *BackLetter* apologize for the error.

References:

BackLetter, Evidence in multiple areas trending against antibiotics for back pain in the presence of Modic changes, 2020; 35(2):21.

Fritzell P et al., Bacteria: back pain, leg pain and Modic sign-a surgical multicenter comparative study. 2019; 28 (12):2981–89.

Pain Problems and Addiction in Rural America

The past several years have seen a modest but gratifying reduction in the prescription of medical opioids in the United States—both in urban and rural areas. However, medical opioid prescription and opioid abuse remain much more common in rural than in urban areas for multiple reasons.

This is a huge concern for rural residents. According to a recent study in *JAMA Network Open*, opioid and other forms of drug abuse, along with economic issues, are among the foremost concerns facing rural adults.

In a large survey of US rural residents by Mary Finding et al., opioid or other drug addiction and abuse was cited by 57% of respondents as a serious problem in their communities. A stunning 49% of respondents said they knew someone who is or has been addicted to opioids. (See Finding et al., 2020.)

As a superb article at National Public Radio station KCRW noted, drug problems in rural areas are no surprise. Bram Sable-Smith penned an article about pain and addiction in rural Necedah, Wisconsin (population 916).

"In many ways, rural communities like Necedah have become the face of the nation's opioid epidemic. Drug overdose deaths are more common by population size in rural areas than in urban ones. And rural doctors prescribe opioids more often by far, despite a nationwide decline in prescribing rates since 2012. Meanwhile, rural Americans have fewer alternatives to treat their very real pain, and they disproportionately lack access to effective addiction medication such as buprenorphine," according to Sable-Smith. (See Sable-Smith, 2019.)

Rural residents are older and in poorer health than their urban peers. And they have more pain problems. Necedah has exactly one overworked, full-time family physician. And many patients in this small community report problems accessing medical care—and paying for it.

A glimpse of the problems of Necedah residents confirms the wisdom of a recent quote from the journal *Nature*. "The current opioid epidemic is a symptom of the fraying of the socio-economic fabric of the rural United States," according to Judith Feinberg. (See Feinberg, 2019.)

Disclosures: None declared.

References:

Feinberg J, Tackle the epidemic, not the opioids, *Nature*, 2019; 573(7773):165. doi:10.1038/d41586- 019-02671-9.

Finding MG et al. Views of rural US adults about health and economic concerns, *JAMA Network Open*, 2020; 3(1):e1918745. doi:10.1001/jamanetworkopen.2019.18745.

Sable-Smith B, In rural areas without pain or addiction specialists, family doctors fill in the gaps, *KCRW Morning Edition*, December, 2019; www.kcrw.com/news/shows/morning-edition/npr-story/786916670.

Do You Find Meaning in Your Life?

A question that is rarely heard in the workup of patients with back pain and related problems is "Do you find meaning in your life?"

Yet the answer to this question may have an important influence on health and personal satisfaction, though it has not been well studied in the back pain area.

Psychiatrist Awais Aftab, MD, and colleagues from the University of California at San Diego performed a cross-sectional study of 1042 adults who are part of the Successful Aging Evaluation study. They keyed on the influence of two factors on health: having meaning in life and searching for meaning in life.

"In our sample, presence [of meaning] positively correlated with physical and mental well-being, and search for meaning negatively correlated with mental well-being and cognitive function, according to Aftab et al. (See Aftab et al., 2019.)

"The medical field is beginning to recognize that meaning in life is a clinically relevant and potentially modifiable factor, which can be targeted to enhance the well-being and functioning of patients," said Aftab in a published statement accompanying the study. "We anticipate that our findings will serve as building blocks for the development of new interventions for patients searching for purpose."

"Many think about the meaning and purpose in life from a philosophical perspective, but meaning in life is associated with better health, wellness and perhaps longevity," said senior author Dilip V. Jeste, MD. "Those with meaning in life are happier and healthier than those without it."

"When you are young, like in your twenties, you are unsure about your career, a life partner and who you are as a person. You are searching for meaning in life," said Jeste.

"As you start to get into your thirties, forties and fifties, you have more established relationships, maybe you are married and have a family and you're settled in a career. The search decreases and the meaning in life increases."

"After age 60, things begin to change. People retire from their job and start to lose their identity. They start to develop health issues and some of their friends and family begin to pass away. They start searching for the meaning in life again because the meaning they once had has changed."

It does not take much imagination to conclude that people with meaningful lives and strong personal direction might be better able to weather the slings and arrows of common pain conditions and avoid becoming disabled by them.

Disclosures: None declared.

Reference:

Aftab A et al., Meaning in life and its relationship with physical, mental, and cognitive functioning, *Journal of Clinical Psychiatry*, 2019; doi:10.4088/JCP.19m13064.

Daunting Challenge

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Whatever diagnostic label they bear, these patients have difficulty tapering opioids and/or discontinuing them altogether. And they often require psychological support, alternative pain therapies, and medication-assisted treatment. They often fail to meet their tapering goals. However, their problems and characteristics fall short of meeting the criteria for OUD or addiction.

This is large body of patients—with estimates ranging from several hundred thousand to several million. Sadly, the US healthcare system is not currently equipped to address their problems adequately—and to provide effective treatment. Unless there is quick action this is a problem that may haunt patients and the healthcare system for years or decades to come.

Complex Tapering Issues and Complex Pain Problems

These people don't just have frustrating tapering problems. They also have complex pain issues which also require effective treatment.

Lembke is a psychiatrist and addiction specialist at Stanford University. "It is essential that we build an infrastructure inside the house of medicine to help the millions of patients struggling with opioid dependence. Public policy to date has addressed opioid addiction and prevention, but the large cohort of patients who are opioid dependent but not addicted has been left behind," she said in a recent email.

"Many of these patients are struggling with the adverse effects of long-term opioid therapy, including the risks of addiction and overdose death. They will need an infusion of resources to support tapering and provide alternative treatments for pain. This is not just an addiction crisis, it is a pain crisis, and I would add it is an iatrogenic opioid-dependence crisis. This latter group has fallen between the cracks of our public policy measures. It's time we recognized the urgent need to support patients who need and would benefit from opioid tapering when medically indicated."

Like Lembke, Chou feels there is an urgent need to move ahead in addressing this crisis—even if it requires filling in some evidence gaps in the future.

"I think it is important to consider this diagnosis even while more research is needed because patients with dependence problems present an important challenge. We are already seeing a lot of these patients. Clinicians are having a hard time knowing what to do with them and how to treat them effectively and safely," said Chou in an email.

"It is essential that we build an infrastructure inside the house of medicine to help the millions of patients struggling with opioid dependence. Public policy to date has addressed opioid addiction and prevention, but the large cohort of patients who are opioid dependent but not addicted has been left behind.

"Many of these patients are struggling with the adverse effects of long-term opioid therapy, including the risks of addiction and overdose death. They will need an infusion of resources to support tapering and provide alternative treatments for pain.

"This is not just an addiction crisis, it is a pain crisis, and I would add it is an iatrogenic opioid-dependence crisis. This latter group has fallen between the cracks of our public policy measures. It's time we recognized the urgent need to support patients who need and would benefit from opioid tapering when medically indicated." —Anna Lembke, MD

"Right now what is mostly happening with people who have a lot of difficulty tapering is: 1) they are labeled as 'problem' patients and may even be discharged for being 'noncompliant,' 2) they are put back on higher doses of opioids, which is risky; or 3) they are given a diagnosis of opioid use disorder [i.e. addiction] which has all sorts of potential impacts in terms of labeling and stigma. As we argue in the article, what we see with prescription opioid dependence is qualitatively different from classic OUD, particularly in relation to illicit use."

Background on Opioid Dependence

Ballantyne and colleagues described the background to opioid dependence in a ground-breaking article in the journal *Pain* in 2019.

"When opioids were first promoted as safe and effective treatment for chronic pain, the argument for safety relied on the [idea] that dependence would reverse within days, and the treatment could be easily stopped after a taper, if necessary. But experience does not bear this out," according to Ballantyne et al. (See Ballantyne et al., 2019).

"Attempts to taper in patients whose opioid therapy has become unhelpful or unsafe have exposed a new problem which we define as: refractory dependence on opioid analgesics. For patients with this condition, tapering is extremely distressing, prolonged, and, in many cases, not tolerated (with the risk that patients seek opioids elsewhere). Early attempts at structuring treatment algorithms for the condition suggest an urgent need to provide a definition and a diagnostic label, so that the appropriate resources can be summoned and not hampered by confused terminology," they added.

Chou pointed out in his email that that the concept of opioid dependence has a long history in medicine. But its meaning has evolved. "The concept of substance or opioid dependence was a separate diagnosis in DSM-IV (i.e., the influential Diagnostic and Statistical Manual of Mental Health Disorders.)" However, it was dropped as an independent diagnosis in the more recent DSM-5.

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Recognizing Prescription Opioid Dependence—Which Differs From Opioid Use Disorder or Addiction

In a recent essay in *Pain*, Jane Ballantyne, MD, and colleagues stressed that complex persistent opioid dependence differs in fundamental respects from opioid addiction, though it can certainly transition into addiction if managed poorly.

"Despite many similarities to opioid addiction, and overlapping symptoms, this complex dependence should be distinguished from addiction, because it is not addiction either neurobiologically, and because it needs treatment that is similar but different from addiction treatment."

Ballantyne and colleagues recently proposed six criteria for the state of "opioid dependence," as outlined in Table I.

Ballantyne believes there will be agreement on a short, standardized definition in the near future. "I think it does lend itself to a single standardized definition. If OUD does, then CPOD is far less amorphous."

Table I. Proposed Criteria for Opioid Dependence

No craving or compulsive use
No harmful use that is not medically directed (patient takes opioids exactly as prescribed)
Withdrawal/drug opposite effects: somatic withdrawal symptoms, hyperalgesia [increased sensitivity to pain], hyperkatefeia [increased sensitivity to emotional distress], dysphoria [profound sense of unease]
Difficulty tapering, possibly lifelong
Stress-like symptoms
Reward deficiency and social withdrawal

Adapted from Ballantyne et al. (2019).

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"For DSM-5 "dependence" and "abuse" were combined into a single entity called 'substance (opioid) use disorder [SUD or OUD].' So the concept of dependence is not new in itself," Chou explained. "The difference is we are mainly defining it in the context of prescription opioid use and tapering because this is where the features of persistent opioid dependence often manifest themselves. There is not much out there yet on prevalence, natural history, etc.," according to Chou. "I am sure there will be some refinement of the definition and criteria over time."

When Gradual Opioid Tapering Becomes a Harrowing Experience

Many patients—hundreds of thousands to millions— taking long-term opioids will end up having to taper their dosages to a safer level—or discontinue opioids altogether. The Centers for Disease Control and Prevention suggests considering gradual tapering when patients:

- Request lower dosages;
- Do not achieve clinically meaningful improvement in pain or function;
- Exhibit substance use disorders;
- Experience overdose or other serious adverse events; and
- Show early warning signs for overdose risk such as confusion, sedation, or slurred speech.

And here is what the CDC means by gradual tapering: "A decrease of 10% per month is a reasonable starting point if patients have taken opioids for more than a year. A decrease of 10% per week may work for patients who have taken opioids for a shorter time (weeks to months)," according to the CDC Pocket Guide on Tapering. (See CDC, 2020).

But according to recent reports, many individuals utilizing long-term opioid therapy appear to be having problems with their tapering programs.

"As tapering experience accrues, clinicians have observed that many patients with chronic pain receiving long-term opioid therapy struggle to reduce doses. Why are tapers a challenge in some patients? An important reason is dependence, characterized by withdrawal symptoms when opioid doses are decreased or discontinued. In addition to somatic symptoms, withdrawal may manifest as psychological symptoms. Even with stable doses, patients can experience continuous subthreshold withdrawal between doses, dysphoria [profound unease], and hyperalgesia [hypersensitivity to pain], all of which can be exacerbated by tapering." according to Chou et al. in *Annals of Internal Medicine*.

Some patients may have to undergo gradual tapering programs for years to scale down to a safer dosage. Some may never reach this goal.

What Does the Emerging Tapering Crisis Mean for Healthcare Providers?

Some healthcare providers reading this *BackLetter* article may be thinking "This won't affect my practice. If my patients develop this distinctive state of dependence, I'll just refer them out to pain and addiction specialists."

That strategy unfortunately is not going to work. There are simply not enough specialists in this area to go around.

This is an issue that will have to be dealt with at a grassroots level, often by

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Daunting Challenge

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hardworking, overburdened primary care practitioners. So everyone in the business of treating chronic back pain and other potential indications for opioid therapy needs to pay careful attention to this emerging issue.

"There is not enough addiction medicine capacity and there is not enough capacity from pain specialists either," Chou reported. "Unfortunately, even if there were capacity, many pain clinics are not enthusiastic about treating patients with pain and addiction or dependence. So I think that much of the burden will fall on primary care physicians (PCPs)."

Broader Use of the Opioid Buprenorphine May Help

As mentioned above, many patients with problematic opioid dependence will require multidisciplinary care. Happily, there is a promising medication option for many patients with problematic opioid dependence that could be employed in that context.

In their article in *Annals of Internal Medicine*, Chou, Ballantyne, and Lembke proposed that physicians consider buprenorphine as a standard treatment option, in the context of broader care.

"As noted in the article, we think buprenorphine is a good option and can be prescribed by PCPs. It is almost certainly a safer drug than pure opioid agonists in this situation," according to Chou. "The problem of course being that it can be used to treat OUD only by clinicians who have a waiver [a special license to prescribe it.], and it is not clear how treating someone diagnosed as having opioid dependence would be viewed by the Drug Enforcement Administration. Regardless—I think it is important for all PCP's to undergo waiver training for buprenorphine—it is a potentially life-saving medication."

Buprenorphine, of course, is itself an opioid. According to the Substance Abuse and Mental Health Services Administration (SAMSHA) it can aid in the treatment of opioid addiction and opioid dependence. It can lower potential for misuse, diminish the effects of physical dependency to opioids, reduce withdrawal symptoms and cravings, and increase safety in cases of overdose.

"This means that, like [other] opioids, it produces effects such as euphoria or respiratory depression at low to moderate doses. With buprenorphine, however, these effects are weaker than full opioid agonists such as heroin and methadone," noted an article at the SAMSHA website.

"Buprenorphine's opioid effects increase with each dose until at moderate doses they level off, even with further dose increases. This "ceiling effect" lowers the risk of misuse, dependency, and side effects. Also, because of buprenorphine's long-acting agent, many patients may not have to take it every day," according to SAMSHA. (See SAMSHA, 2020).

However, to dispense buprenorphine, physicians, physician assistants, and nurse practitioners must complete an eight-hour training course and apply for a waiver from SAMSHA.

They are only allowed to treat 30 patients in the first year. Only then can they apply to increase their patient limit.

Relatively Few US Physicians Prescribe Buprenorphine at the Moment

Unfortunately, at the moment only about 10% of US primary care providers (MDs, physician assistants, and nurse practitioners] have a waiver to offer buprenorphine treatment at the moment. So there is a need for a major effort to train and license these primary care providers—or a revision in buprenorphine prescription regulations.

Either way, this is going to be a long uphill struggle.

Disclosures: None declared.

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Ballantyne J et al., Refractory dependence on opioid analgesics, *Pain*, 2019; 160(12):2655–60. doi:10.1097/j.pain.0000000000001680.

CDC, Pocket Guide: Tapering Opioids for Chronic Pain; www.cdc.gov/drugoverdose/pdf/Clinical_Pocket_Guide_Tapering-a.pdf.

Chou R et al., Rethinking opioid dose tapering, prescription opioid dependence, and indications for buprenorphine [published online ahead of print August 27, 2019], *Annals of Internal Medicine*; doi:10.7326/M19-1488.

Krebs EE, Evaluating consequences of opioid prescribing policies [published online ahead of print January 2, 2020], *Journal of General Internal Medicine*; doi:10.1007/s11606-019-05600-8.

SAMSHA, Buprenorphine; https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine.

Mindless Back Care Costs

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These researchers compared administrative healthcare costs in two very different systems: (1) the multipayer system in the United States and (2) the single-payer system in Canada. They utilized a variety of financial data sources.

US insurers and providers spent $812 billion on administration, amounting to $2497 per capita (34.2%) vs. $551 per capita (17% in Canada). This translated into the following breakdowns in overheads: $844 vs. $146 in terms of insurers' overheads; $933 vs. $196 for hospital administration; $255 vs. $123 for nursing home, home care, and hospice administration; and $465 vs. $87 for physicians' insurance-related costs.

These two countries had similarly structured healthcare systems until the early 1970s when Canada adopted a single-payer system. Before that juncture the two systems employed similar numbers of administrative personnel: 43.8/10,000 population in the United States and 40.8/10,000 in Canada.

The researcher found that the administrative costs of overall US health spending rose by 3.2 percentage points between 1999 and 2017, from 31.0 % to 34.2%. Of the 3.2-percentage point increase, most (2.4 percentage points) was due to the expanding role that private insurers have assumed in tax-funded programs such as Medicaid and Medicare. Private insurers' increasing involvement has pushed up overhead in those public programs; private Medicare Advantage plans take 12% or more of premiums for their overhead, whereas traditional Medicare's overhead is just 2%, a difference of at least $1155 per enrollee (per year).

If the United States provided significantly better health care services than Canada, these costs might be justifiable.

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Universities, Hospitals, and Governments Cheating on Reporting Study Results

In 2017 the US government began requiring researchers and institutions to report clinical trial results within a year of study completion.

However, compliance with that regulation is shoddy in the extreme, according to a study in the *Lancet*. From 2017 through September 2019 only 41% of completed clinical trials reported results by the one-year legal deadline. And there is no sign of progress in this effort. The proportion of clinical trials reporting by the legal deadline has been in a stall since mid-2018.

Distilling the Evidence Base Across Medicine

So why is that a significant problem? "Failure to report the results of a clinical trial can distort the evidence base for clinical practice, breaches researchers' ethical obligations to participants, and represents an important source of research waste," said Nicolas DeVito, MD, and colleagues in the *Lancet*.

"Patients and clinicians cannot make informed choices about which treatments work best when trial results are routinely withheld. Clinical trials are not abstract research projects: they are large, expensive, practical evaluations that directly impact on patient care by informing treatment guidelines and evidence reviews." said senior author Ben Goldacre, MD, in a statement at the *Lancet* website.

"Sponsors are breaching their legal obligations, but also their ethical obligations to the patients who generously participate in clinical trials. Our study has identified over 2,400 trials breaching the rules, but to our knowledge, the FDA has never levied a single fine or other enforcement action, despite all the levers available to them. Compliance will only improve when action is taken."

The US Government Hasn't Punished Any Offenders

The regulation, part of the 2017 FDA Amendments Act, authorized penalties of $10,000 per day for offending institutions, healthcare companies, and researchers. Yet, as mentioned above, the US government has not yet levied a single penalty.

"Patients and clinicians cannot make informed choices about which treatments work best when trial results are routinely withheld. Clinical trials are not abstract research projects: they are large, expensive, practical evaluations that directly impact on patient care by informing treatment guidelines and evidence reviews." —Ben Goldacre, MD.

"Over four decades since non-reporting of clinical trials was first reported, it is disappointing to see that we have only progressed to legislation being passed, and then largely ignored," says DeVito. "The fact that the US Government cannot comply with its own laws is particularly concerning."

"Until effective enforcement action is taken, public audit may help. We have established an openly accessible public website at fdaaa.trialstracker.net where fresh data on compliance with FDAAA will be posted every day, identifying each individual overdue trial, and compliance statistics for each individual sponsor. We hope this will help to incentivize sponsors and provide useful targeted information for all those who aim to comply with the law," according to DeVito.

Drug and Device Industries Not the Worst Offenders

So who are the worst offenders in terms of not reporting clinical trial results in a timely manner? Some might suspect that the drug and device industries would be slow to respond to the new regulation. And industry has been slow in responding to this regulation. But drug and device companies did not have the worst track records.

That award went to universities, the US government, and other non-industry sponsors. Trials with an industry sponsor were much more likely to comply with the law than those with a non-industry or US Government sponsor (50% vs 34% vs 31% trials submitted in time), according to DeVito and colleagues.

Better performance was also seen among sponsors with more experience of running large numbers of trials, when compared with those who have only ever run a very small number of projects (66% vs 21% trials submitted in time).

Enforcement of the Law Would Make a Major Difference

In an accompanying editorial, Erik von Elm, MD, and Joerg J. Meerpohl, MD lamented a lost opportunity. "Any law is only as good as its enforcement...if this rule were to be enforced, academic sponsors would probably make substantial efforts to reduce the number of non- or late-reported trials and to improve data quality. Training, auditing, and incentive mechanisms could be overseen by dedicated staff. A senior 'transparency officer' versed in trial conduct and reporting could take a proactive mentoring role and help investigators overcome barriers that currently prevent them from timely reporting of trial results in registries. If completeness of reporting was a criterion in individual academic evaluations, this could have a considerable 'signaling effect' within the local research community."

Disclosures: None declared.

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Vito N, Compliance with legal requirement to report clinical trial results on ClinicalTrials.gov: A cohort study, published online January 17, 2020; https://doi.org/10.1016/S0140-6736(19)33220-9.

Von Elm E and Meerpohl JJ, Trial results reporting: FDA Amendments Act Final Rule needs enforcement, published online January 17, 2020; https://doi.org/10.1016/S0140-6736(20)30105-7.

MEETING CALENDAR

- **47th Annual Meeting, International Society for the Study of the Lumbar Spine, Combined with SpineWeek, 2020**
  April 27-May 1, 2020
  Melbourne, Australia
  Contact: Katarina Olinder Eriksson, Administator, ISSLS
  c/o Institute of Clinical Sciences
  Sahlgrenska Academy
  University of Gothenburg
  PO Box 426 SE-405 30
  Gothenburg, Sweden
  Tel: 46-31-786-44-36
  E-mail: katarina.olinder@gu.se

- **International Association for the Study of Pain 2020 World Pain Congress**
  August 4-8, 2020
  Amsterdam, The Netherlands
  Contact: IASP
  1510 H Street NW, Suite 600
  Washington, DC 20005
  Tel: 202-856-7400
  Fax: 202-856-7401

- **Eurospine 2020**
  October 7-9, 2020
  Vienna, Austria
  Contact: Eurospine, Spine Society of Europe
  Attn: Judith Reichert
  Schild Seefeldstrasse 16
  8610 Uster-Zurich,
  Switzerland
  Tel: 41-44-994-1404
  www.eurospinemeeting.org

- **NASS 2020: Annual Meeting of the North American Spine Society**
  October 7-10, 2020
  San Diego, California
  Contact: North American Spine Society
  7075 Veterans Boulevard
  Burr Ridge, IL 60527
  Tel: 630-230-3600
  Fax: 630-230-3700
  www.spine.org

Coming Soon:

- **What is Usual Care for Low Back Pain Around the World?**
- **Why Hasn't Medicine Done a Better Job of Documenting Usual Care?**
- **Slight Increase in Life Expectancy in the United States: Opioid-Related?**
- **Open-Label, Obvious Placebos Reduce Pain and Disability**
- **Inflammation in Non-Specific Back Pain**

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"Americans spend twice as much per person as Canadians on health care. But instead of buying better care, that extra spending buys us sky-high profits and useless paperwork. Before their single-payer reform, Canadians died younger than Americans, and their infant mortality rate was higher than ours. Now Canadians live three years longer and their infant mortality rate is 22% lower than ours," said lead author Himmelstein in a published statement accompanying the study.

These authors are proponents of Medicare for All, a proposed system where a single public agency or combination public/private agency would coordinate care. This would lead to an instant reduction in administrative costs and overheads.

"Americans spend twice as much per person as Canadians on health care. But instead of buying better care, that extra spending buys us sky-high profits and useless paperwork."
—David Himmelstein, MD

"Medicare for All could save more than $600 billion each year on bureaucracy, and repurpose that money to cover America's 30 million uninsured and eliminate copayments and deductibles for everyone," according to senior author Steffie Woolhandler. (See PNHP, 2020.)

Disclosures: None declared.

References:

Himmelstein DU et al., Health care administrative costs in the United States and Canada, 2017 [published online ahead of print January 6, 2020], *Annals of Internal Medicine*; doi:10.7326/M19-2818.

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THE BACK*PAGE*

Testosterone Still Overhyped as a Treatment

Testosterone remains widely hyped as a treatment for diminished libido, fatigue, loss of vitality, malaise, perceived loss of strength and fitness—and even low back pain.

In the wake of heavy direct-to-consumer advertising, testosterone sales tripled from 2001 to 2011 and then sagged somewhat after two studies linked testosterone replacement with elevated risk of heart attack and stroke.

The American College of Physicians (ACP) hopes to take the wind out of the overuse of testosterone therapy. After a recent systematic review on age-related decline in testosterone levels, the ACP recommended that physicians should prescribe testosterone therapy only to treat sexual dysfunction.

"Physicians are often asked by patients about low 'T' and are skeptical about the benefits of testosterone treatment," according to ACP President Robert M. McLean, MD. "The evidence shows that men with age-related low testosterone may experience slight improvements in sexual and erectile function. The evidence does not support prescribing testosterone for men with concerns about energy, vitality, physical function, or cognition."

What about routine screening for low testosterone (or "Low-T" as it is often called in TV and radio ads)?

"Given that testosterone's effects were limited to small improvements in sexual and erectile function in men with low testosterone levels, it is unlikely that screening men for low testosterone levels or treating men without sexual or erectile dysfunction and low testosterone levels would be effective."

This review did not address testosterone therapy as a treatment for hypogonadism, for which there is a different body of evidence. (*See Annals of Internal Medicine*, 2020; https://annals.org/aim/fullarticle/2758507/testosterone-treatment-adult-men-age-related-low-testosterone-clinical-guideline.)

"Power of the Bad": Negativity Bias and the Back Pain Crisis

Prominent psychology researcher Roy Baumeister, PhD, recently penned a highly touted book with John Tierney on "Power of the Bad"—about the human tendency to overreact to bad and worrisome events and information.

"The power of the bad goes by several names in the academic literature: the negativity bias, negativity dominance, or simply the negativity effect. By any name it means the universal tendency for negative events and emotions to affect us more strongly than positive ones."

This tendency is firmly rooted in the evolution of humans and human brains. Think of the hypervigilance that might protect a hunter against a saber-toothed tiger. But it still has profound effects in the modern world.

When humans become overly reactive to the bad, they often end up in a perpetual state of crisis, exacerbated by a round-the-clock barrage of negative information in the mass media.

"By continually fomenting fears, the prophets of doom have profoundly distorted the public's view of the present and the future. By hyping small or nonexistent threats to induce panicky responses, they create far more problems than they solve," according to Baumeister and Tierney.

And negativity bias almost certainly has played a role in the modern back pain crisis—by making patients and healthcare providers overly fearful of missing important pathology and unrecognized diseases. The continuing overutilization of imaging and diagnostic procedures for back symptoms would appear to support that interpretation. As would the continuing overreaction to asymptomatic abnormalities on imaging scans.

This likely played a role in the development of the opioid overtreatment crisis. In the 1990s, there was a common assertion that the prescription of opioids could *prevent* the transition from acute to chronic back pain without undue risk for most patients. That, of course, played to the fears of people with acute pain, with devastating results. (*See* Baumeister RF and Tierney J, *The Power of Bad*. New York, NY: Penguin Press, 2019.)

Drugstore Chains Implicated in Opioid Crisis Now Blaming MDs

States and other entities around the United States have sued drugstore chains and drug distributors for their contributions to the devastating opioid overdose crisis—suggesting they should have recognized the growing impact of opioid medications on their patients.

"More than 2,500 cities, counties, Native American tribes and other groups have filed federal lawsuits against companies throughout the drug industry over the epidemic, which has resulted in the overdose deaths of more than 400,000 people over the past two decades," according to a *Washington Post* article by Lenny Bernstein.

However, drugstore chains are striking back, asserting they acted legally as intermediaries in the prescriptions that licensed MD wrote. They suggest they acted simply as toll collectors in filling legal prescriptions and that the real culprits in this tragic series of events were the physicians who wrote them.

"Major drugstore chains—which face an October trial in the mammoth federal opioid litigation—have sued doctors across northeast Ohio, claiming that physicians are the real culprits in the nation's deadly drug epidemic," Bernstein noted.

This will certainly complicate this massive litigation effort.

There are, of course, many culpable parties in this huge medical debacle, including drugstore chains, opioid wholesalers, and physicians. (*See Washington Post*, January 8, 2020; www.washingtonpost.com/health/major-drugstore-chains-sue-doctors-in-sprawling-federal-opioid-case/2020/01/07/3ac9cd70-317d-11ea-9313-6cba89b1b9fb_story.html.)

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