THE JOURNAL of the AMERICAN OSTEOPATHIC ASSOCIATION

The Journal of the American Osteopathic Association (*JAOA*) encourages osteopathic physicians, faculty members and students at colleges of osteopathic medicine, and others within the health care professions to submit comments related to articles published in the *JAOA* and the mission of the osteopathic medical profession. The *JAOA*'s editors are particularly interested in letters that discuss recently published original research.

Letters must be submitted online at http://www.osteopathic.org/JAOAsubmit. Letters to the editor are considered for publication in the *JAOA* with the understanding that they have not been published elsewhere and are not simultaneously under consideration by any other publication. All accepted letters to the editor are subject to editing and abridgment.

Although the *JAOA* welcomes letters to the editor, these contributions have a lower publication priority than other submissions. As a consequence, letters are published only when space allows.

The OSTEOPATHIC Trial Demonstrates Significant Improvement in Patients With Chronic Low Back Pain as Manifested by Decreased Prescription Rescue Medication Use

To the Editor:

It was interesting to read the article by Prinsen and colleagues regarding osteopathic manipulative treatment (OMT) of patients with low back pain in the February 2014 issue of *The Journal of the American Osteopathic Association*.[1] The authors are to be commended for seeking to implement a more pragmatic and efficient alternative to the conventional randomized controlled trial for efficacy of OMT. However, in using the American Osteopathic Association Clinical Assessment Program (AOA-CAP) data, the authors introduced several biases and limitations into their methodology. Consequently, their conclusions were inconsistent with current best evidence on OMT in the management of chronic low back pain.

The most critical methodological questions raised by the authors following their study were whether a visual analog scale (VAS) score for pain may be too insensitive to reveal the potentially statistically significant advantages of managing low back pain with OMT and whether the potentially confounding effects of medication use for low back pain can be adequately controlled in a randomized controlled trial. Apparently, the authors were unaware of the results of the OSTEOPAThic Health outcomes In Chronic low back pain (OSTEOPATHIC) Trial, which squarely address each question. The OSTEOPATHIC Trial used a randomized, double-blind, sham-controlled design to assess OMT efficacy in 455 patients,[2] thereby making it the largest trial to address such questions. Therein, a VAS was used to demonstrate statistically significant and clinically relevant pain improvement with OMT in patients with chronic low back pain.[3] In fact, VAS pain scores were sufficiently robust to demonstrate a large OMT effect in the subgroup of patients with moderate to severe levels of baseline low back pain.[4]

Beyond these statistically significant and clinically relevant pain reductions with OMT in the OSTEOPATHIC Trial, it was also shown that patients in the OMT group less frequently used prescription medication for low back pain than did patients in the sham OMT group, even after controlling for multiple potential confounders.[3] Notably, in the OSTEOPATHIC Trial (unlike the AOA-CAP program), medication for low back pain was independently prescribed by physicians who were not part of the investigative team and, therefore, were blinded to patient treatment allocation. The results of the OSTEOPATHIC Trial are consistent with representative, population-based data from the National Ambulatory Medical Care Survey indicating that osteopathic physicians manage low back pain by prescribing medications, particularly nonsteroidal anti-inflammatory drugs, less frequently than allopathic physicians.[5]

There were several other methodological issues in the authors' study that deserve further comment. First, given the large number of graduates of colleges of osteopathic medicine who have entered residency programs approved by the Accreditation Council

for Graduate Medical Education,[6] family medicine residencies approved by the AOA are not likely to be truly representative of osteopathic medical care. Second, because the participation rate of invited family medicine residencies was not reported, selection bias may exist even within the subgroup of AOA-approved residencies. Third, because the randomization process for selecting patient medical records within residency programs was not strictly overseen by the investigators, it cannot simply be assumed to have been validly performed. Fourth, only 55% of eligible patients had both initial and final VAS scores for low back pain. It is unclear why imputation for missing data was not attempted to include the remaining proportion of study patients. Fifth, physicians at the participating residency programs potentially provided both prescription medication and OMT for low back pain, each in an unblinded fashion. This methodology raises serious questions about internal validity, particularly regarding the fundamental relationships among VAS pain scores, prescribing of analgesic medication, and provision of OMT.

Finally, the rationale for the AOA recommendation of abstracting 20 medical records per residency program to ensure adequate sample size and statistical power is not described and likely does not adequately address the clustering of observations within practice-based research networks. Parenthetically, such clustering is aggravated by the fact that only 27 family medicine residencies were needed to acquire 1013 medical records, rather than the 51 residencies that would have been needed with strict adherence to the 20-record limit. Failure to recognize clustering causes dramatically under-powered studies. Subsequent failure to adequately adjust for such clustering yields unrealistically precise treatment effects,[7] which inflate the type 1 error rate and bring statistically significant results into question. Unfortunately, the variance inflation factor needed to correct for clustering relating to OMT within clinics can be quite high, as recently demonstrated by the Consortium for Collaborative Osteopathic Research Development–Practice-Based Research Network (CONCORD-PBRN).[8] For example, in comparison with the sample size for a population-based study of individual patients, 20- to 40-fold increases in sample size may be needed to validly assess the use of various OMT techniques among patients within a small group of networked clinics.

In summary, despite the consistency of the authors' results with those of a randomized controlled trial by Andersson and colleagues,[9] both study results are at odds with current best evidence. The OSTEOPATHIC Trial has clearly shown that OMT provides statistically significant and clinically relevant pain improvement in patients with chronic low back pain as further manifested by the decreased need for prescription rescue medication. (doi:10.7556/jaoa.2014.103)

John C. Licciardone, DO, MS, MBA

The Osteopathic Research Center, University of North Texas Health Science Center (UNTHSC), Fort Worth; Department of Medical Education, UNTHSC Texas College of Osteopathic Medicine, Fort Worth

References

1. Prinsen JK, Hensel KL, Snow RJ. OMT associated with reduced analgesic prescribing and fewer missed work days in patients with low back pain: an observational study. *J Am Osteopath Assoc.* 2014;114(2): 90-98. doi:10.7556/jaoa.2014.022.
2. Licciardone JC, King HH, Hensel KL, Williams DG. OSTEOPAThic Health outcomes In Chronic low back pain: the OSTEOPATHIC Trial. *Osteopath Med Prim Care.* 2008;2:5. doi:10.1186/1750-4732-2-5.
3. Licciardone JC, Minotti DE, Gatchel RJ, Kearns CM, Singh KP. Osteopathic manual treatment and ultrasound therapy for chronic low back pain: a randomized controlled trial. *Ann Fam Med.* 2013;11(2):122-129. doi:10.1370/afm.1468.
4. Licciardone JC, Kearns CM, Minotti DE. Outcomes of osteopathic manual treatment for chronic low back pain according to baseline pain severity: results from the OSTEOPATHIC Trial [published online June 10, 2013]. *Man Ther.* 2013;18(6):533-540. doi:10.1016/j.math.2013.05.006.
5. Licciardone JC. The epidemiology and medical management of low back pain during ambulatory medical care visits in the United States. *Osteopath Med Prim Care.* 2008;2(1):11. doi:10.1186/1750-4732-2-11.
6. Brotherton SE, Etzel SI. Graduate medical education, 2012-2013 [appendix]. *JAMA.* 2013;310(21):2328-2346. doi:10.1001/jama.2013.278364.
7. Dickinson LM, Basu A. Multilevel modeling and practice-based research. *Ann Fam Med.* 2005;3(suppl 1):S52-S60.
8. Licciardone JC, Kearns CM, King HH, et al. Somatic dysfunction and use of osteopathic manual treatment techniques during ambulatory medical care visits: A CONCORD-PBRN study. *J Am Osteopath Assoc.* 2014;114(5):344-354. doi:10.7556/jaoa.2014-072.
9. Andersson GB, Lucente T, Davis AM, Kappler RE, Lipton JA, Leurgans S. A comparison of osteopathic spinal manipulation with standard care for patients with low back pain. *New Engl J Med.* 1999;341(19):1426-1431.

(continued)

Response: Observational Study Demonstrates That OMT Is Associated With Reduced Analgesic Prescribing and Fewer Missed Work Days

We read with interest the comments of Dr Licciardone[1] on our recent publication from the February 2014 edition of the *The Journal of the American Osteopathic Association* (*JAOA*) entitled, "OMT [Osteopathic Manipulative Treatment] Associated With Reduced Analgesic Prescribing and Fewer Missed Work Days: An Observational Study." We are grateful to have the opportunity to respond.[2]

We believe that Dr Licciardone's comments fall into 2 broad categories: first, a restatement of the limitations of the article—and of observational studies in general—and second, a summarization of how findings of the OSTEOPAThic Health outcomes In Chronic low back pain (OSTEOPATHIC) Trial relate to our findings.

We commend Dr Licciardone on his recent publications, including the OSTEOPATHIC Trial; however, we feel obliged to point out that the 2 studies he most frequently cites, and the studies on which he relies most heavily for his comments on our publication, were unpublished[3] or in press[4] when our manuscript was accepted for publication. Therefore, it would have been impossible for us to reference these studies in our article. We believe that our original publication is corroborated by these studies, with the exception of the pain scores. In response to a critique of an article he authored, Dr Licciardone himself noted in 2013 that research leads to "evolving standards of evidence" that would be difficult to predict if established after the original publication.[5] In building an evidence base, each publication is a brick, and together, the bricks establish a solid foundation for clinical decision-making. The authors of each publication reference and build on the best literature available at the time their work is completed. The literature, which is constantly evolving, must periodically be reviewed and summated.

Dr Licciardone also notes "methodological issues" in our study.[1] Observational studies such as ours[2] certainly have their limitations, which we believe we discussed thoroughly in our article. Indeed, our limitations section addressed missed data and each potential bias. We encourage readers to review our study[2] for a detailed summary of our study's limitations and methodology.

It is important to note that our study examined the relationship between patients who received OMT by osteopathic physicians and those who did not. Our study did not attempt to compare OMT to allopathic care for low back pain and, therefore, we do not regard Dr Licciardone's comments[1] comparing our study to a study with different comparators as relevant or a valid critique. The large number of graduates from colleges of osteopathic medicine in recent years does not logically lead one to conclude that the care residents administer is not representative of the osteopathic medical profession. We agree that the data represent a specific subset of osteopathic physicians, as we discussed originally in our article, and the data should be interpreted accordingly.

One of the limitations of our study was that only 55% of patients had both initial and final visual analog scores recorded.[2] In the corresponding letter to the editor,[1] it was noted, "It is unclear why imputation for missing data was not attempted to include the remaining proportion of study patients." *Imputation,* or the use of estimated values for missing data, can be attractive to researchers because it is conceptually simple and the resulting sample set has the same number of observations as the complete data set. It can be very appealing when analysis eliminates a large proportion of the data; however, this method of analysis has limitations. Some imputation methods result in biased parameter estimates (eg, means and correlations), unless the data are missing completely at random. The bias is often worse than that with complete-case analysis, especially with the use of imputations based on a mean. The extent to which the bias affects the final analysis is dependent on several factors; yet, all imputation methods underestimate standard errors. It is important to remember that imputed observations are themselves estimates, and their values contain corresponding random error. In light of this fact, imputed values are treated as actual observations for the purpose of statistical analyses. The additional source of error is ignored, resulting in falsely depressed errors and *P* values. Furthermore, although imputation is possible, it is usually difficult to do well in practice and is not ideal in most instances. Indeed, current Consolidated Standards of Reporting Trials (ie, CONSORT guidelines) discourage the commonly used last-observation-carried-forward method of imputation.[6]

Dr Licciardone[1] points to the potential bias related to clustering, yet he fails to men-

tion that we addressed this potential bias in our publication.[2] Although clustering would theoretically increase the type 1 error rate, it would also, if true, decrease the strength of the statistical difference and imply a false positive finding. Ironically, this theory would suggest that OMT does not alter workdays, prescribing patterns, and pain.

Although randomized controlled trials (RCTs) may continue to be the gold standard of research, their time and financial commitment places them out of reach for many physicians. Most physicians have limited resources and time, as they are primarily appointed to clinical positions. However, these physicians can meaningfully contribute to medical research by using alternative study designs, such as case studies, observational studies, and retrospective studies. These study designs have an important niche within research, each with their respective strengths and weaknesses.

Increasingly, funding organizations, such as the Patient-Centered Outcomes Research Institute (http://www.pcori.org/), are focusing on actual patient outcomes rather than results from RCTs. This shift is in response to some of the limitations of RCTs and the generalizability of their results to broad populations. The use of actual patient outcomes in research will increasingly require the use of pseudoexperimental designs to answer questions affecting both policy and payment. Registries such as the American Osteopathic Association Clinical Assessment Program have the ability to contribute in a meaningful way to these decisions, and in some cases registries may be the only way to gain knowledge about health services delivery. In light of this shift, the profession needs to stand behind the accurate, consistent collection of data, which reduces bias introduced by missing data points, and work together to combine results from various studies of osteopathic care in a seamless way for decision makers. This process, which ultimately results in guidelines for care, can ensure that the value of osteopathic care is recognized.

As scientists, we are obligated to be objective and report findings of our investigations, regardless of whether they corroborate the findings of other studies. Our study demonstrated that patients with low back pain who received OMT had a decrease in the prescription of analgesic medications, fewer nerve-blocking injections, and fewer reported missed or limited-duty days of work. These findings of decreased analgesic medication use in patients who receive OMT concur with previous findings from a major RCT.[7] Separating the interaction between use of manipulation, use of pain medications, and patient outcomes of reduced pain and improved functionality would have been difficult with any study design. Our findings of the associations between the use of manipulation and the reduction in pain, as measured by the surrogates of analgesia prescription and increased functionality, reinforce previous findings and demonstrate the value of OMT in managing low back pain. (doi:10.7556/jaoa.2014.104)

Joseph K. Prinsen, DO, PhD
Department of Medicine, Vanderbilt University Medical Center, Vanderbilt School of Medicine, Nashville, Tennessee

Kendi L. Hensel, DO, PhD
Department of Osteopathic Manipulative Medicine, University of North Texas Health Science Center Texas College of Osteopathic Medicine, Fort Worth

Richard J. Snow, DO, MPH
Ohio Health, Columbus; Department of Family Medicine, Ohio University Heritage College of Osteopathic Medicine at Athens

References

1. Licciardone JC. The OSTEOPATHIC Trial demonstrates significant improvement in patients with chronic low back pain as manifested by decreased prescription rescue medication use [letter]. *J Am Osteopath Assoc.* 2014;114(7):528-529. doi:10.7556/jaoa.2014.103.
2. Prinsen JK, Hensel KL, Snow RJ. OMT associated with reduced analgesic prescribing and fewer missed work days in patients with low back pain: an observational study. *J Am Osteopath Assoc.* 2014;114(2):90-98. doi:10.7556/jaoa.2014.022.
3. Licciardone JC, Kearns CM, Minotti DE. Outcomes of osteopathic manual treatment for chronic low back pain according to baseline pain severity: results from the OSTEOPATHIC Trial [published online June 10, 2013]. *Man Ther.* 2013;18(6):533-540. doi:10.1016/j.math.2013.05.006.
4. Licciardone JC, Kearns CM, King HH, et al. Somatic dysfunction and use of osteopathic manual treatment techniques during ambulatory medical care visits: A CONCORD-PBRN study. *J Am Osteopath Assoc.* 2014;114(5):344-354. doi:10.7556/jaoa.2014-072.
5. Licciardone JC. Systematic review and meta-analysis conclusions relating to osteopathic manipulative treatment for low back pain remain valid and well accepted. *J Bodyw Mov Ther.* 2013;17:2-4.
6. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomized trials. *BMJ.* 2010;340:c869. doi:10.1136/bmj.c869.
7. Andersson G, Lucente T, Davis AM, Kappler RE, Lipton JA, Leurgans S. A comparison of osteopathic spinal manipulation with standard care for patients with low back pain. *N Engl J Med.* 1999;341(19):1426-1431.

A Case of Seasonal Recurrent Myopericarditis? Tough to Say!

To the Editor:

We read with great interest the case report by Divoky and Wilford[1] published in the January 2014 issue of *The Journal of the American Osteopathic Association*. The authors described a case of an intermittent relapsing form of recurrent myopericarditis that appeared to have a seasonal correlation. The authors referred to it as *seasonal recurrent myopericarditis*.

Although it was an interesting and well-written report, we would like to highlight our observations about the case. The first and subsequent symptoms of recurrent pericarditis can often occur at variable times after the initial attack, but symptoms usually recur within 18 months.[2,3] Arbitrarily, a 6-week period is used to differentiate 2 forms of recurrent pericarditis: intermittent relapsing form (in which patients may have symptom-free intervals of more than 6 weeks without therapy) and incessant form (in which discontinuation of anti-inflammatory therapy always results in symptoms within 6 weeks).[3] The use of corticosteroids as a first-line treatment in acute pericarditis is one of the strongest risk factors for future episodes of relapsing pericarditis and reduces the efficacy of colchicine.[3-6] The early use of steroids may augment viral replication, thus causing increased viral antigen exposure in viral or idiopathic pericarditis and thus increasing the risk for relapsing pericarditis.[3-6] In the presented case,[1] the patient was discharged while taking oral steroids (for unclear reasons) after his first attack of viral myopericarditis, despite clinical improvement with nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine. The oral steroids could have triggered the patient's recurrent symptoms. With the exception of underlying connective tissue disease, ongoing steroid use, pregnancy, or previously demonstrated failure of the standard therapy (NSAIDs or colchicine), steroids are rarely the initial choice of therapy in patients with acute pericarditis.[4]

Additionally, patients with previous herpes infection (especially herpetic pericarditis) can have symptoms similar to recurrent pericarditis (similar to Mollaret meningitis), especially patients with an immunocompromised status. Although herpetic pericarditis appeared unlikely for the described patient for the reasons the authors described, this possibility should be remembered.

The authors stated, "From an immunologic standpoint, the seasonal aspect of this case does not necessarily support a viral etiologic process because immunity would develop after the first illness—unless a different organism was responsible each time."[1] We disagree with this statement. Idiopathic pericarditis is often viral in nature, and at least 15% to 20% of patients experience a recurrence.[3] Another example of a potential viral etiologic process is a reactivation of the herpes infection in patients with herpetic pericarditis.

One additional differential consideration to the presented case is drug-induced myopericarditis, as suggested by the paroxysmal use of cannabis in this patient (confirmed with positive drug screen results). Cannabis is a known potential trigger for the recurrence of pericarditis by inducing inflammation.[7] We believe that it is possible that a combination of these triggers may have played a role in the patient's recurrent symptoms, rather than a mere seasonal preponderance as defined. (doi:10.7556/jaoa.2014.105)

Lovely Chhabra, MD

Department of Cardiovascular Medicine, Hartford Hospital, University of Connecticut School of Medicine

Vinod K. Chaubey, MD

David H. Spodick, MD, DSc

Department of Medicine, Saint Vincent Hospital, University of Massachusetts Medical School, Worcester

References

1. Divoky L, Wilford RD. A case of seasonal recurrent myopericarditis. *J Am Osteopath Assoc*. 2014;114(1):52-55. doi:10.7556/jaoa.2014.007.
2. Imazio M, Demichelis B, Parrini I, et al. Management, risk factors, and outcomes in recurrent pericarditis. *Am J Cardiol*. 2005;96(5):736-739.
3. Chhabra L, Spodick DH. Pericardial disease in the elderly. In: Aronow WS, Fleg JL, Rich MW, eds. *Tresch and Aronow's Cardiovascular Disease in the Elderly*. 5th ed. Boca Raton, FL: CRC Press; 2014:644-668.
4. Chhabra L, Spodick DH. Letter by Chhabra and Spodick regarding article, "Treatment of acute and recurrent idiopathic pericarditis." *Circulation*. 2013;128(19):e391. doi:10.1161/CIRCULATIONAHA.113.003737.
5. Imazio M, Trinchero R. Myopericarditis: etiology, management, and prognosis [published online January 24, 2008]. *Int J Cardiol*. 2008;127(1):17-26. doi:10.1016/j.ijcard.2007.10.053.
6. Artom G, Koren-Morag N, Spodick DH, et al. Pretreatment with corticosteroids attenuates the efficacy of colchicine in preventing recurrent pericarditis: a multi-centre all-case analysis [published online August 8, 2005]. *Eur Heart J*. 2005;26(7):723-727.
7. Jouanjus E, Leymarie F, Tubery M, Lapeyre-Mestre M. Cannabis-related hospitalizations: unexpected serious events identified through hospital databases. *Br J Clin Pharmacol*. 2011;71(5):758-765. doi:10.111/j.1365-2125.2010.03897.x.

Response

We appreciate the comments and expertise of Chhabra et al.[1] The interesting aspect of our case[2] was the timing of the recurrent symptoms. For 3 consecutive years, the patient received a diagnosis of myopericarditis within the same 4-week period of the calendar year—with a potential fourth episode the following year—and no symptoms in the intervening periods.[2] The timing of our patient's recurring symptoms certainly fell inside the usual period for recurring myopericarditis symptoms, which, as Chhabra et al state, is typically within 18 months of the original episode.[1,3] However, the recurrent annual presentation such as the one described in our case[2] has not been previously reported in the literature, to our knowledge. By definition, seasonal occurrence is occurrence at the same time of the year. An example of a disorder with seasonal occurrence is *seasonal affective disorder*, which is depression that occurs during a specific season of the year, most often winter.[4] On the basis of this definition, we believe our description of "seasonal recurrent myopericarditis" is accurate.

We agree with Chhabra et al[1] that early oral steroid use could have been associated with the recurrent episodes of pericarditis in our patient. After the first incident of myopericarditis, the patient's symptoms partially improved with naproxen. Colchicine was added to the patient's treatment regimen because of the severity of his symptoms. Colchicine, as an adjunct to nonsteroidal anti-inflammatory drugs or aspirin, is the first line of treatment for patients with recurrent pericarditis and, according to recent research, should also be considered for first line of treatment for patients with acute pericarditis.[5,6] Ideally, the patient would have continued to receive colchicine after discharge but, unfortunately, he was unable to afford the cost of colchicine and was not eligible for the patient assistance program available at that time. For this reason, the patient was prescribed oral corticosteroids after 2 days of receiving colchicine as an inpatient.

We also agree with Chhabra et al[1] that a viral cause was likely in our patient. Our statement that "the seasonal aspect of this case does not necessarily support a viral etiologic process"[2] should be revised, as it was not meant to refute a viral cause of our patient's recurrent myopericarditis. In fact, the seasonal pattern could be related to a virus that circulates in late fall, with subtle antigenic differences each year.

Chhabra et al[1] also proposed cannabis-induced myopericarditis as a potential differential consideration in our case. This consideration is interesting and, although it is a possibility, the patient in our case intermittently smoked cannabis throughout the year, not just during the time of the recurrent myopericarditis, making this cause less likely. A recent publication postulated the causality of recurrent myopericarditis to contaminated cannabis use.[7] In that case, the individual smoked contaminated cannabis 48 to 72 hours before the onset of symptoms.[7] Our patient intermittently used cannabis and did not have a recurrence of symptoms after every use as described in the mentioned case report.

In conclusion, the exact etiologic process of our patient's myopericarditis may never be determined. However, the annual recurrence of symptoms within the same 4-week time frame, with no symptoms in the intervening periods, certainly fits the definition of "seasonal." (doi:10.7556/jaoa.2014.106)

Laura Divoky MD

Rex D. Wilford DO

Department of Internal Medicine,
Summa Health System, Akron, Ohio

References

1. Chhabra L, Chaubey VK, Spodick DH. A case of seasonal or recurrent viral myopericarditis? tough to say [letter]! *J Am Osteopath Assoc.* 2014;114(7):532. doi:10.7556/jaoa.2014.105.
2. Divoky L, Wilford RD. A case of seasonal recurrent myopericarditis. *J Am Osteopath Assoc.* 2014;114(1):52-55. doi:10.7556/jaoa.2014.007.
3. Imazio M, Demichelis B, Parrini I, et al. Management, risk factors, and outcomes in recurrent pericarditis. *Am J Cardiol.* 2005;96(5):736-739.
4. Oren DA, Koziorowski M, Desan PH. SAD and the not-so-single photoreceptors. *Am J Psychiatry.* 2013;170(12):1403-12. doi:10.1176/appi/ajp.2013.13010111.
5. Imazio M, Brucato A, Cemin R, et al; ICAP Investigators. A randomized trial of colchicine for acute pericarditis [published online August 31, 2013]. *N Engl J Med.* 2013;369(16):1522-1528. doi:10.1056/NEJMoa1208536.
6. Imazio M, Belli R, Brucato A, et al. Efficacy and safety of colchicine for treatment of multiple recurrences of pericarditis (CORP-2): a multicentre, double-blind, placebo-controlled, randomised trial [published online March 28, 2014]. *Lancet.* doi:10.1016/S0140-6736(13)62709-09.
7. Rodríguez-Castro CE, Alkhateeb H, Elfar A, Saifuddin F, Abbas A, Siddiqui T. Recurrent myopericarditis as a complication of marijuana use. *Am J Case Rep.* 2014;15:60-62. doi:10.12659/AJCR.889808.