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Statin Myopathy

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Interoperability

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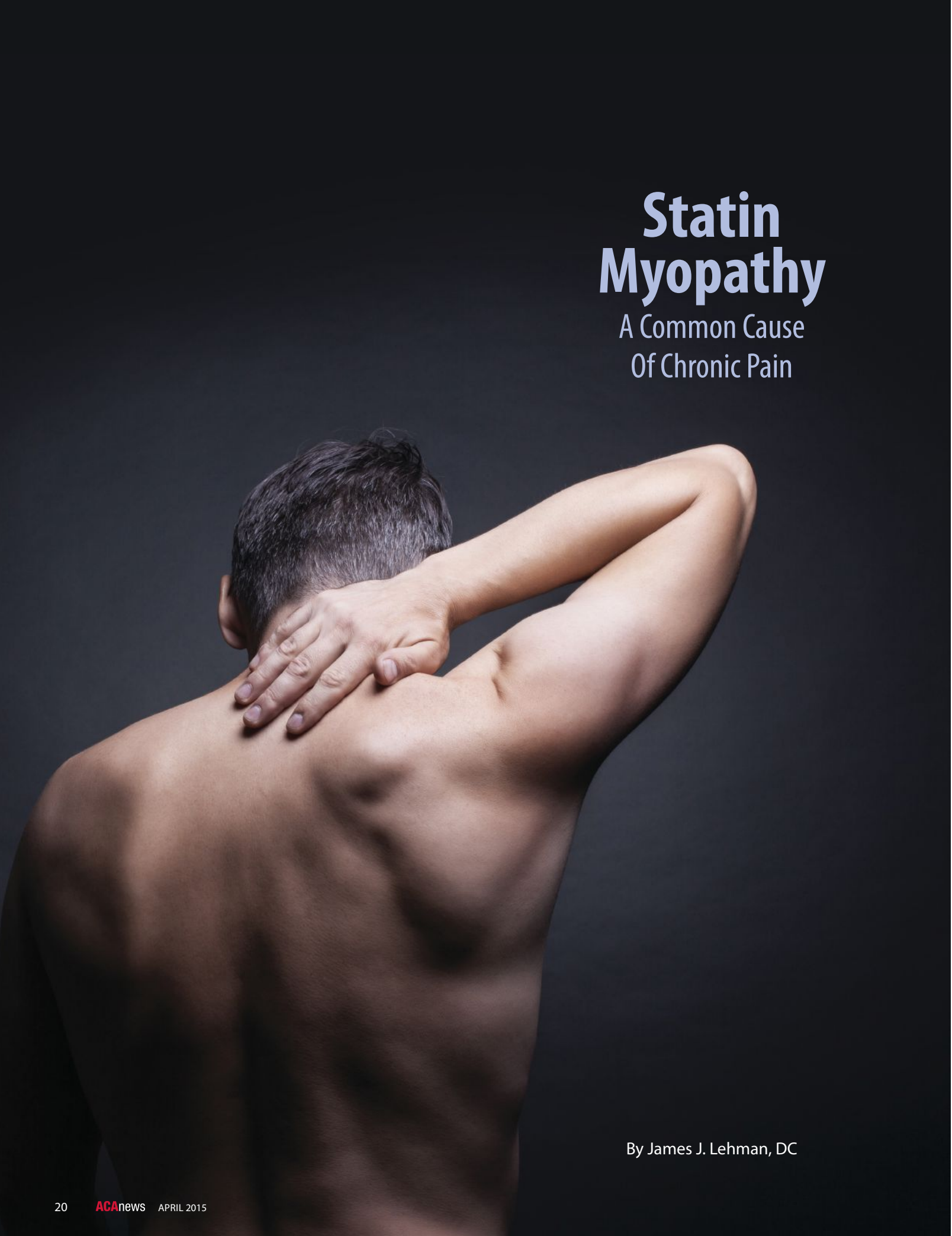
A Common Cause Of Chronic Pain



By James J. Lehman, DC

Statin myopathy is a common dilemma that causes persistent myalgia[1] and chronic pain. Chiropractic physicians should be prepared to evaluate patients with these conditions. This article describes statin myopathy and its differential diagnosis.

While primary care physicians and chiropractic physicians treat more than 90 percent of chronic pain patients in the United States,[2] the treatment approaches vary considerably. Primary care providers, such as allopathic and osteopathic physicians, advanced practice registered nurses and physician assistants often focus on pharmacological therapeutics, including the use of opioids. Chiropractic physicians focus on nonpharmacological therapeutics to relieve pain due to neuromusculoskeletal conditions, which as of January 2015 are included in the standard of care promulgated by the Joint Commission.[3] As a member of the medical staff for a federally qualified health center, credentialed as a patient-centered medical home, I appreciate the Joint Commission's new standards. There is a need to revolutionize the treatment of chronic pain in America,[4] and nonpharmacological therapeutics, including chiropractic and acupuncture interventions, are reasonable solutions.

The Community Health Center Inc. of Middletown, Conn. has integrated chiropractic services into nine primary care sites. Chiropractic specialists and chiropractic residents (e.g., nonsurgical orthopedics and neuromusculoskeletal medicine) evaluate and manage chronic pain patients as members of the primary care team. As one of the chiropractic specialists, I have encountered chronic pain patients who do not respond favorably to pharmacological care offered by primary care providers or the nonpharmacological chiropractic treatment. Often these non-responsive patients are taking statins to prevent heart attacks and death.[5] So now I consider statin myopathy as a possible cause of chronic pain. Since my training and scope of practice do not include pharmacological therapeutics, I do not alter the patient's medications, but as an evidence-based and patient-centered provider, I have a responsibility to the patient and the primary care provider to communicate my diagnosis. Because I'm a member of the medical staff with full access to the electronic health care record, I am able to efficiently communicate my concerns to the prescribing primary care provider.

Since the majority of chiropractic physicians practice as solo practitioners or as associates in chiropractic practices,[6] they face a conundrum when a chronic pain patient presents with the symptoms of statin myopathy. It is common for prescribing physicians to deny drug toxicity and the symptoms of statin myopathy.[7] Although a doctor of chiropractic (DC) is capable of performing focused history and neuromusculoskeletal examination, which is essential when evaluating muscle complaints that may be induced by statins, the diagnosis is complicated for the chiropractic physician because the process usually involves a change in the statin prescription or a "statin holiday," which is not within the chiropractic scope of practice. However, a DC does have the ability to contact the patient's medical provider to discuss the statin and work with that provider on behalf of the patient.

Statin Therapy Guidelines

The Centers for Disease Control and Prevention estimated in 2010 that 32 million Americans take statin medications. 50 percent of men between 65 and 75 years of age and 39 percent of women ages 75 and older were taking statins from 2005 to 2008. One in four Americans over 45 years of age take statin medications.[8] New guidelines, formulated by the American Heart Association and the American College of Cardiology, would increase the use of statins for the older population to 87 percent of men ages 60 to 75 and 54 percent of women in that age range.[9]

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The new guidelines recommend statin therapy for the following groups:[10]

- People without cardiovascular disease who are 40 to 75 years old and have a 7.5 percent or higher risk for having a heart attack or stroke within 10 years.
- People with a history of a cardiovascular event (e.g., heart attack, stroke, stable or unstable angina, peripheral artery disease, transient ischemic attack, or coronary or other arterial revascularization).
- People 21 and older who have a very high level of bad cholesterol (i.e., 190 mg/dL or higher).
- People with Type 1 or Type 2 diabetes who are 40 to 75 years old.

Incidence of Statin Myopathy

For several reasons, controlled clinical trials underestimate the actual percentage of patients who suffer statin myopathy and suggest that muscle problems are rare.[11] Observational studies in nonselected outpatients show a higher frequency of muscle complaints in the statin groups than in the control groups. Statin myopathy frequency has been reported at 9 to 20 percent with these studies. By some estimates, statin myopathy affects 7 million of the 33 million people taking statins in the United States, or 25 percent of the cases.[12]

In spite of the following warning offered by *Consumer Reports* regarding the use of statin medications, it appears that prescribing physicians usually reject any possible connection of statins and symptoms supported by evidence in the literature.

> *If you are taking a statin and have muscle aches, pain or weakness, call your doctor right away. This could be a sign of a dangerous breakdown in the muscle tissue.*

A patient-targeted survey, addressing how physicians responded when patients presented with possible adverse drug reactions (ADRs) to statin medications, demonstrated that physicians usually do not acknowledge patients' complaints including muscle pain.

> *87 percent of patients reportedly spoke to their physician about the possible connection between statin use and their symptom. Patients reported that they and not the doctor most commonly initiated the discussion regarding the possible connection of drug to symptom (98% vs 2% cognition survey, 96% vs 4% neuropathy survey, 86% vs 14% muscle survey; $p < 10^{-8}$ for each). Physicians were reportedly more likely to deny than affirm the possibility of a connection. Rejection of a possible connection was reported to occur even for symptoms with strong literature support for a drug connection, and even in patients for whom the symptom met presumptive literature-based criteria for probable or definite drug-adverse effect causality. Assuming that physicians would not likely report ADRs in these instances, these patient-submitted ADR reports suggest that targeting patients may boost the yield of ADR reporting systems.*[13]

Costs

Consumer Reports Best Buy Drugs lists a significant variation in costs for statin medications. In 2007, a generic statin costs as little as $12 per month or less, with brand-name statin costs escalating to more than $500 per month.[14] Normally, these medications are prescribed for long-term use, and cost is relevant for patients. Of interest is that up to 60 percent of patients discontinue use of statins within two years of the initial prescription.[15]

Key Points

A panel of four physicians, including three cardiologists and one neuroscientist, claims that statins are effective but underprescribed because of muscle toxicity concerns by physicians. The panel offers the following key points regarding statin myopathy:[16]

- *There is little consensus on the definition of statin-induced myopathy, and it is underdiagnosed.*
- *Abnormal pharmacokinetic activity contributes to toxicity, but some patients may be predisposed by underlying metabolic muscle disorders.*
- *A focused history and neuromusculoskeletal examination are important in the evaluation of muscle complaints that may be induced by statins.*
- *In patients with possible statin-induced myopathy, assessing the risks and benefits of statin therapy is essential.*
- *For patients who cannot tolerate statin therapy, alternatives include a "statin holiday" followed by a rechallenge with a different statin, intermittent rosuvastatin (Crestor) or resin therapy. Sometimes the best alternative is a compromise between the goal level for low-density-lipoprotein cholesterol and the level achievable with alternative therapy.*

Definitions

ACUTE CORONARY SYNDROME: The term refers to any group of clinical symptoms compatible with acute myocardial ischemia and includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI).[28]

MYALGIA: Muscle weakness, soreness, tenderness, stiffness, cramping or aching, either at rest or with exercise, without elevation of creatine kinase (CK).

MYOSITIS: Elevated CK with or without muscle symptoms. The "itis" suffix is unfortunate since myositis does not correspond to inflammation on biopsy.

RHABDOMYOLYSIS: Muscle symptoms with a CK level 10 times the upper limit of normal or higher. Evidence of renal dysfunction is not required for the diagnosis, as pre-existing renal disease and hydration status are more closely related to kidney damage than the degree of muscle injury.[29]

Pharmacokinetic Activities

In 1997, Lennemas and Fager described the pharmacodynamics and pharmacokinetics of the HMG-CoA reductase inhibitors and pointed out the similarities and differences. They explained the crucial role of hypercholesterolemia and the subsequent development of coronary heart disease and atherosclerosis and its risks of progression with increasing levels of total serum cholesterol or low-density lipoprotein (LDL) cholesterol.

> *The statins are reversible inhibitors of the microsomal enzyme HMG-CoA reductase, which converts HMG-CoA to mevalonate. This is an early rate-limiting step in cholesterol biosynthesis. Inhibition of HMG-CoA reductase by statins decreases intracellular cholesterol biosynthesis, which then leads to transcriptionally upregulated production of microsomal HMG-CoA reductase and cell surface LDL receptors.*[17]

Adverse Effects

The FDA added a safety warning about associated cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment and confusion) and the numerous interactions with cardiovascular and other drugs that may increase the toxicity of statins.[18] There are also increased risks of raised blood sugar levels and the development of Type 2 diabetes. Some drugs interact with statins in a way that increases the risk of muscle injury (myopathy), characterized by unexplained muscle weakness and/or pain.

Statin-Associated Muscle-Related Adverse Effects

In one case series involving 354 patients (age range 34-86 years) who self-reported muscle-related problems associated with statin therapy, 93 percent of the patients reported muscle pain, 88 percent fatigue and 85 percent weakness.[19] Patients with persistent muscle pain due to statin myopathy present with symptoms of muscle weakness, soreness, tenderness, stiffness, cramping or aching, either at rest or with exercise.[20] It is common for women taking statins to experience exertional fatigue and loss of energy.[21] In my experience, many patients suffering with chronic pain present with similar nonspecific muscle symptoms. Warren Hammer, DC, claims his patients complain of nonspecific muscle pain, tenderness, weakness, joint pains, peripheral neuropathy, tendinopathy and lupus-like symptoms that may be caused by the use of cholesterol-lowering drugs (statins).[22]

Differential Diagnosis

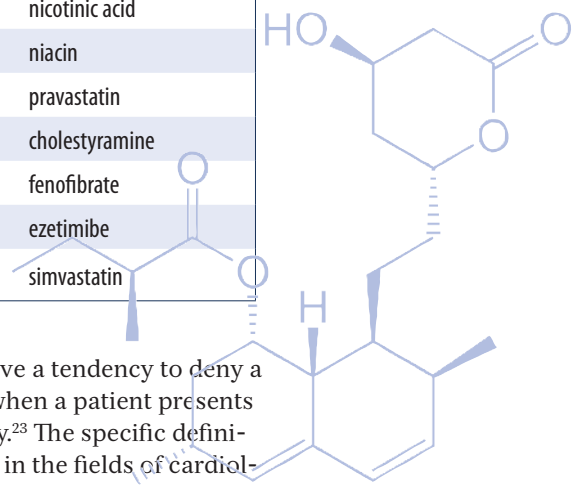
It is essential that specific definitions differentiate the types of statin myopathy. While myositis and rhabdomyolysis must be recognized and treated immediately, physicians have a tendency to deny a possible drug connection when a patient presents with myalgia or neuropathy.[23] The specific definitions developed by experts in the fields of cardiology, statin myopathy and drug toxicity attempt to clarify three different statin-associated muscle-related adverse effects: myalgia, myositis and rhabdomyolysis.[24]

A case report described two chiropractic patients presenting with chief concerns of neuromusculoskeletal pain complaints while taking statins. The first patient sought relief of pain in the neck, both legs and knees. The other patient presented with a chief concern of lower thoracic paraspinal pain. Both of these patients responded favorably with a statin holiday and a change in statin medications respectively.[25] The chiropractic physician did not advise the patients to discontinue their medications but referred them to their prescribing physicians.

Statin myopathy patients may present for chiropractic care complaining of chronic neuromusculoskeletal pains affecting the spine and/or extremities. Often there is no history of recent trauma. Provocative maneuvers may or may not reproduce the pains of chief concern. Conservative chiropractic treatments may provide only temporary relief or no relief of the persistent muscle or nerve pain. I suggest that whenever a patient presents with persistent muscle pain and a history of statin medications, you consider statin myopathy as a cause of the chronic pain.

Brand Names and Generic Names of Cholesterol-Lowering Drugs[26]

Brand Name	Generic Name
Atromid-S	clofibrate
Colestid	colestipol
Crestor	rosuvastatin
Lescol	fluvastatin
Lipitor	atorvastatin
Lopid	gemfibrozil
Mevacor	lovastatin
Niacin	nicotinic acid
Niaspan	niacin
Pravachol	pravastatin
Questran: Questran Light	cholestyramine
Tricor	fenofibrate
Zetia	ezetimibe
Zocor	simvastatin



Discussion

Patients suffering with musculoskeletal pain frequently present to chiropractic clinicians for evaluation and management.[27] The rising use of statins indicates that an increasing number of patients suffering with muscle pain, neurological symptoms and chronic pain due to statin toxicity will present to primary care providers and chiropractic clinicians. Hence, chiropractic physicians might be better prepared to evaluate patients with statin myopathy if the chiropractic colleges teach that to chiropractic students and graduates.

Chiropractic students, as part of their training, are taught to perform a differential diagnosis in order to determine the cause of the patient's neuromusculoskeletal pain symptoms. The students determine the pain generator and its cause through the process of differential diagnosis, involving a focused history and physical examination. It is necessary to discuss the pharmacology and pharmacokinetics of statins. The need to communicate directly with the prescribing provider and the patient is stressed to the students. I suggest that evidence-based and patient-centered care mandates that when the neuromusculoskeletal complaints are due to statin myopathy, the attending chiropractic physician should advise the patient and the prescribing provider of these clinical concerns.

I suggest that the majority of chiropractic clinicians may not recognize this drug-induced muscle pain. It would be enlightening to receive feedback from chiropractic clinicians. So, I pose the following question collectively to the readers of this manuscript: "Would you recognize a patient with statin myopathy if he or she walked into your office?" Please respond to my email: *jlehman@bridgeport.edu.* ■

Endnotes

1 Fernandez G, Spatz ES, Jablecki C, and Phillips PS. Statin myopathy: a common dilemma not reflected in clinical trials. *Cleveland Clinic Journal of Medicine*, Vol 78, Number 6. June 2011.

2 Blondell RD and Ashrafioun L. Treating Opioid Dependency and Coexistent Chronic Nonmalignant Pain. *Am Fam Physician.* 2008 Nov 15;78(10):1132-1133.

3 Revisions to pain management standard effective January 1, 2015. Standard PC.01.02.07: The [organization] assesses and manages the [patient's] pain. *Joint Commission Online.* Nov. 12, 2014. Available from: *www.jointcommission.org/assets/1/23/jconline_November_12_14.pdf.* [See Jan/Feb *ACA News*, Page 8]

4 The Mayday Fund. A Call To Revolutionize Chronic Pain Care in America: An Opportunity for Health Care Reform.

5 Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005; 366:1267–1278.

6 For the Good of the Patient: The Integrative Chiropractor. *ACA News.* Available from: *www.acatoday.org/content_css.cfm?CID=3298.*

7 Golomb BA, McGraw JJ, Evans, MA Dimsdale, JE 2007. "Physician Response to Patient Reports of Drug Adverse Effects: Implications for Patient-Targeted Adverse Effect Surveillance." *Drug Safety*; 30(8): 669-675.

8 Wehrwein P. Statin use is up, cholesterol levels are down: Are Americans' hearts benefiting? *Harvard Health Blog.* Available from: *www.health.harvard.edu/blog/statin-use-is-up-cholesterol-levels-are-down-are-americans-hearts-benefiting-201104151518.*

9 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. *J Am Coll Cardiol.* Volume 63, Issue 25, Practice Guideline July 2014.

10 Doctor discussion is key for cholesterol treatment. American Heart Association. *Blog.heart.org.* Available from: *http://blog.heart.org/doctor-discussion-is-key-for-cholesterol-treatment.*

11 Ganga HV, Slim HB and Thompson PD. A systematic review of statin-induced muscle problems in clinical trials. *Am Heart J.* 2014 Jul;168(1):6-15. doi: 10.1016/j.ahj.2014.03.019. Epub 2014 Apr 12.

12 Vladutiu GD. Genetic predisposition to statin myopathy. *Curr Opin Rheumatol.* 2008;20-648-655.

13 Golomb BA, McGraw JJ, Evans, MA Dimsdale, JE 2007. "Physician Response to Patient Reports of Drug Adverse Effects: Implications for Patient-Targeted Adverse Effect Surveillance." *Drug Safety*; 30(8): 669-675.

14 Choosing a Statin to Lower Cholesterol. *Consumer Reports Health Best Buy Drugs.*

15 Jackevicius CA, Mamdani M, Tu JV. Adherence of Statin Therapy in Elderly Patients with and without acute coronary syndromes. *JAMA* 2002;288:462-467.

16 Fernandez G, Spatz ES, Jablecki C, and Phillips PS. Statin myopathy: a common dilemma not reflected in clinical trials. *Cleveland Clin J Med*, Vol 78, Number 6. June 2011.

17 Lennemas H, Fager G. Pharmacodynamics and pharmacokinetics of the HMG-CoA reductase inhibitors. Similarities and differences. *Clin Pharmacokinet.* 1997 May;32(5). 403-425.

18 United States Food and Drug Administration FDA drug safety communication: important safety label changes to cholesterol-lowering statin drugs. Silver Spring (MD): The Food and Drug Administration; 2012. Available from: *www.fda.gov/Drugs/DrugSafety/ucm293101.htm.*

19 Cham S, Evans MA, Denenberg JO, Golumb BA. Statin-associated muscle-related adverse effects: a case series of 354 patients. *Pharmacotherapy.* 2010 Jun;30(6):541-53. doi: 10.1592/phco.30.6.541.

20 Linares LA, Golomb BA, Jaojoco JA, Sikand H, Phillips PS. The modern spectrum of rhabdomyolysis: drug toxicity revealed by creatine kinase screening. *Curr Drug Saf.* 2009 Sep;4(3):181-7. Epub 2009 Sep 1.

21 Golomb BA, Evans MA, Dimsdale JE, White HL. Effects of Statins on Energy and Fatigue With Exertion: Results From a Randomized Controlled Trial. *Arch Intern Med*/Vol 172 (NO. 15), Aug 13/27, 2012: 1180-1182

22 Hammer W. That Persistent Muscle Pain May Be Drug-Induced. *Dynamic Chiropractic* – Feb. 24, 2003, Vol. 21, Issue 05.

23 Golomb BA, McGraw JJ, Evans, MA Dimsdale, JE 2007. "Physician Response to Patient Reports of Drug Adverse Effects: Implications for Patient-Targeted Adverse Effect Surveillance." *Drug Safety*; 30(8): 669-675.

24 Linares LA, Golomb BA, Jaojoco JA, Sikand H, Phillips PS. The modern spectrum of rhabdomyolysis: drug toxicity revealed by creatine kinase screening. *Curr Drug Saf.* 2009 Sep;4(3):181-7. Epub 2009 Sep 1.

25 Rodine RJ, Tibbles AC, Kim PSY, Alikhan N. Statin induced myopathy presenting as mechanical musculoskeletal pain observed in two chiropractic patients. *J Can Chiropr Assoc.* Mar 2010; 54(1): 43–51.

26 Cholesterol Lowering Drugs. Cleveland Clinic. Available from: *http://my.clevelandclinic.org/health/diseases_conditions/hic_Cholesterol/hic_About_Cholesterol-Lowering_Drugs.*

27 Chiropractic: An Introduction. National Center for Complementary and Integative Health (NCCIH). *http://nccam.nih.gov/health/chiropractic/introduction.htm.*

28 Kumar A and Cannon CP. Acute Coronary Syndromes: Diagnosis and Management, Part I. *Mayo Clin Proc.* Oct 2009; 84(10): 917–938.

29 Linares LA, Golomb BA, Jaojoco JA, Sikand H, Phillips PS. The modern spectrum of rhabdomyolysis: drug toxicity revealed by creatine kinase screening. *Curr Drug Saf.* 2009 Sep;4(3):181-7. Epub 2009 Sep 1.

NNT for Statins vs. the Mediterranean Diet

By Shereen K. Lehman, DC, MS and James Lehman, DC

THE NUMBER NEEDED TO TREAT (NNT) represents an estimate of the number of people who need to undergo the treatment of interest in order to prevent one additional adverse outcome from occurring. For example, if an intervention has an NNT of 10, it means you'd have to treat 10 people with that specific intervention to prevent one additional bad outcome.

As a measurement, the NNT is considered to be more clinically useful than sorting through relative risks, odds ratios or absolute risk reduction.[1] But it's important to understand the population that was studied and what the specific outcome of interest is. For example, a medication used to prevent heart attacks from occurring will have one NNT for people who have never had a heart attack but probably a different NNT when it's used for people who are trying to prevent a second incident.

The NNT is typically included in the results of research studies and reviews. An organization called The NNT Group reviews various therapies and diagnostic interventions and lists the findings on its website, *thennt.com*.

NNTs and Statins

Time frame matters too. According to The NNT Group, statin drugs given for five years, in order to prevent heart disease in people who have no history of heart disease, is 104.[2] That means that 104 people have to take statins in order to prevent one extra person from having a heart attack. The NNT Group calculates the number needed to harm (NNH) as well. According to its findings, one in 50 people on statins develops diabetes and one in ten experiences muscle damage as defined as rhabdomyolysis. Undiagnosed muscle pain, such as myalgia, wasn't included.

The picture changes when considering patients who have a history of heart disease. In this case, according to the reviewers, the statins NNT is 83 in order to prevent an additional death from occurring and 39 for preventing a nonfatal heart attack.[3] The harms are the same as in the previous instance.

In comparison, the Mediterranean diet has been studied in a large randomized trial and is included on The NNT website. When followed for five years, the Mediterranean diet has an NNT of 61 for preventing stroke, heart attack or death with no harms noted.[4] So, according to The NNT, the Mediterranean diet appears to be a better choice than statins for primary prevention of stroke, heart attack or death.

When the focus is shifted to studies on patients who've had one heart attack and are trying to prevent a second one, the NNT for the Mediterranean diet drops even lower. In fact, the NNT for preventing that repeat heart attack is 18, and the overall NNT for preventing death or cancer in this group is 30.[5] ■

Endnotes

1 Centre for Evidence-Based Medicine. Number Needed to Treat (NNT). *www.cebm.net/number-needed-to-treat-nnt*

2 The NNT. Statins for Heart Disease Prevention (Without Prior Heart Disease). *www.thennt.com/nnt/statins-for-heart-disease-prevention-without-prior-heart-disease*

3 The NNT. Statins for Heart Disease Prevention (With Known Heart Disease). *www.thennt.com/nnt/statins-for-heart-disease-prevention-with-known-heart-disease*

4 The NNT. Mediterranean Diet for Heart Disease Prevention (Without Known Heart Disease). *www.thennt.com/nnt/mediterranean-diet-for-heart-disease-prevention-without-known-heart-disease/*

5 The NNT. Mediterranean Diet for Post Heart-Attack Care. *www.thennt.com/nnt/mediterranean-diet-for-post-heart-attack-care/*