

10. European Trial on Reduction of Cardiac Events With Perindopril in Stable Coronary Artery Disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet*. 2003;362(9386):782-788.
11. Hou FF, Zhang X, Zhang GH, et al. Efficacy and safety of benazepril for advanced chronic renal insufficiency. *N Engl J Med*. 2006;354(2):131-140.
12. Rouleau JL, Wamica WJ, Baillet R, et al; IMAGINE (Ischemia Management With Accupril Post-Bypass Graft via Inhibition of the Converting Enzyme) Investigators. Effects of angiotensin-converting enzyme inhibition in low-risk patients early after coronary artery bypass surgery. *Circulation*. 2008;117(1):24-31.
13. PEACE Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med*. 2004;351(20):2058-2068.
14. Lüders S, Schrader J, Berger J, et al; PHARAO Study Group. The PHARAO study: prevention of hypertension with the angiotensin-converting enzyme inhibitor ramipril in patients with high-normal blood pressure: a prospective, randomized, controlled prevention trial of the German Hypertension League. *J Hypertens*. 2008;26(7):1487-1496.
15. PREAMI Investigators. Effects of angiotensin-converting enzyme inhibition with perindopril on left ventricular remodeling and clinical outcome: results of the randomized Perindopril and Remodeling in Elderly with Acute Myocardial Infarction (PREAMI) Study. *Arch Intern Med*. 2006;166(6):659-666.
16. Asselbergs FW, Diercks GF, Hillege HL, et al; Prevention of Renal and Vascular Endstage Disease Intervention Trial (PREVEND IT) Investigators. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. *Circulation*. 2004;110(18):2809-2816.
17. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack [published corrections appear in *Lancet*. 2001;358(9292):1556 and *Lancet*. 2002;359(9323):2120]. *Lancet*. 2001;358(9287):1033-1041.
18. Pitt B, O'Neill B, Feldman R, et al; QUIET Study Group. The QUinapril Ischemic Event Trial (QUIET): evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. *Am J Cardiol*. 2001;87(9):1058-1063.
19. Gliddon AE, Doré CJ, Black CM, et al. Prevention of vascular damage in scleroderma and autoimmune Raynaud's phenomenon: a multicenter, randomized, double-blind, placebo-controlled trial of the angiotensin-converting enzyme inhibitor quinapril. *Arthritis Rheum*. 2007;56(11):3837-3846.
20. Oosterga M, Voors AA, Pinto YM, et al. Effects of quinapril on clinical outcome after coronary artery bypass grafting (the QUO VADIS Study). *Am J Cardiol*. 2001;87(5):542-546.
21. Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of enalapril and losartan in type 1 diabetes. *N Engl J Med*. 2009;361(1):40-51.
22. Wang N, Zheng Z, Jin HY, Xu X. Treatment effects of captopril on non-proliferative diabetic retinopathy. *Chin Med J (Engl)*. 2012;125(2):287-292.
23. Patel A; ADVANCE Collaborative Group. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet*. 2007;370(9590):829-840.
24. Beckett NS, Peters R, Fletcher AE, et al; HYVET Study Group. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med*. 2008;358(18):1887-1898.
25. Maschio G, Alberti D, Janin G, et al; Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. *N Engl J Med*. 1996;334(15):939-945.
26. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD; Collaborative Study Group. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. *N Engl J Med*. 1993;329(20):1456-1462.
27. MacMahon S, Sharpe N, Gamble G, et al; PART-2 Collaborative Research Group. Randomized, placebo-controlled trial of the angiotensin-converting enzyme inhibitor, ramipril, in patients with coronary or other occlusive arterial disease. *J Am Coll Cardiol*. 2000;36(2):438-443.
28. Teo KK, Burton JR, Buller CE, et al. Long-term effects of cholesterol lowering and angiotensin-converting enzyme inhibition on coronary atherosclerosis: the Simvastatin/Enalapril Coronary Atherosclerosis Trial (SCAT). *Circulation*. 2000;102(15):1748-1754.
29. Barzilay JI, Davis BR, Cutler JA, et al; ALLHAT Collaborative Research Group. Fasting glucose levels and incident diabetes mellitus in older nondiabetic adults randomized to receive 3 different classes of antihypertensive treatment: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Arch Intern Med*. 2006;166(20):2191-2201.
30. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) [published corrections appear in *JAMA*. 2003;289(2):178 and *JAMA*. 2004;291(18):2196]. *JAMA*. 2002;288(23):2981-2997.
31. Chowdhury EK, Owen A, Ademi Z, et al; Second Australian National Blood Pressure Study Management Committee. Short- and long-term survival in treated elderly hypertensive patients with or without diabetes: findings from the Second Australian National Blood Pressure study. *Am J Hypertens*. 2014;27(2):199-206.
32. Wing LM, Reid CM, Ryan P, et al; Second Australian National Blood Pressure Study Group. A comparison of outcomes with angiotensin-converting-enzyme inhibitors and diuretics for hypertension in the elderly. *N Engl J Med*. 2003;348(7):583-592.
33. Dahlöf B, Sever PS, Poulter NR, et al; ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet*. 2005;366(9489):895-906.
34. Bulpitt CJ, Beckett NS, Cooke J, et al; Hypertension in the Very Elderly Trial Working Group. Results of the pilot study for the Hypertension in the Very Elderly Trial. *J Hypertens*. 2003;21(12):2409-2417.
35. Yui Y, Yuyoshi T, Kodama K, et al; JMIB-B Study Group. Comparison of nifedipine retard with angiotensin converting enzyme inhibitors in Japanese hypertensive patients with coronary artery disease: the Japan Multicenter Investigation for Cardiovascular Diseases-B (JMIB-B) randomized trial. *Hypertens Res*. 2004;27(3):181-191.
36. Bosch J, Yusuf S, Pogue J, et al; HOPE Investigators. Use of ramipril in preventing stroke: double blind randomised trial. *BMJ*. 2002;324(7339):699-702.
37. Dagenais GR, Yusuf S, Bourassa MG, et al; HOPE Investigators. Effects of ramipril on coronary events in high-risk persons: results of the Heart Outcomes Prevention Evaluation Study. *Circulation*. 2001;104(5):522-526.
38. Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients [published correction appears in *N Engl J Med*. 2000;342(10):748]. *N Engl J Med*. 2000;342(3):145-153.

<http://dx.doi.org/10.1016/j.mayocp.2016.04.020>

Decisive Bearing of Organizational Dynamics on the Application and Success of Hospital-Based Cardiac Rehabilitation



To the Editor: Analyses and reviews regarding cardiac rehabilitation (CR) are frequently featured in top-tier journals.^{1,2} Cardiac rehabilitation is a comprehensive secondary prevention program involving exercise training as well as medical evaluation, cardiac risk factor modification, education, and counseling.¹ It been established as one of 9 performance measures for patients with ischemic heart disease by the American College of Cardiology Foundation and other preeminent medical organizations,³ and it has growing relevance amid present-day surges of obesity, sedentariness,

multimorbidity, aging, and other complexities of care for a growing spectrum of patients.^{1,4} Yet, CR underutilization remains entrenched. Logistic (eg, excessive distance and/or lack of transportation) and cost (eg, unaffordable copayments) impediments are often cited as key deterrents.⁴ Many suggest that new models of care (particularly home-based CR) are essential to overcome imbedded obstacles.^{4,5}

Although most CR analyses have focused on patient-specific factors affecting CR utilization, we investigated facility and organizational differences under the premise that there may still be unidentified modifiable organizational, local institutional, and personnel structures that influence enrollment and participation. By examining these relationships, we aimed to identify features conducive to utilization.

Methods. The Veterans Health Administration has 35 hospital-based CR programs among its 124 hospital facilities with inpatient cardiovascular services.⁶ Severe underuse (only 8.4%) of hospital-based CR by veterans eligible for CR has been described previously.⁶ Using administrative data, we found wide variations in utilization of CR across the different Veterans Health Administration facilities with CR programs. We identified 3 high-enrolling and 3 low-enrolling sites with similar complexity characteristics. Using a qualitative study design, we conducted semistructured interviews with a diverse range of patients and health care professionals (up to 4 of each) from each site to characterize features of high and low utilization. In each of the 6 programs, we spoke with patients who did and did not enroll, hospital cardiology staff (cardiologists, hospitalists, nurses), and CR staff (cardiologists, nurses, physical therapists, and exercise specialists) to clarify organizational and contextual barriers to and facilitators of CR utilization.

Results. Our results revealed important differences distinguishing high-enrolling vs low-enrolling sites. Patients from high-enrolling sites uniformly described participating because of strong health care professional endorsement. In contrast, patients from low-enrolling sites who did not enroll could not recall being informed about the program; most did not know the program even existed. Even if these patients were told and forgot, their statements suggest there was something ineffective about the messages they received. Health care professionals from high-enrolling sites uniformly described distinctive organizational climates in relation to CR, ie, there were coherent and uniform messages regarding the value and importance of CR as part of standard care and/or there were organizational processes in place to systematize CR referrals. They also described close working relationships between the cardiology and CR programs. In facilities with low enrollment, cardiology services and CR services were relatively less programmatically aligned. Cardiology staff described limited and sometimes even tense interactions with the CR service, particularly when CR was not managed by cardiology staff.

Although several patients at high-enrolling sites described distance as being a potential barrier to CR, these logistic impediments were generally offset by perceptions that CR had great value, that a spouse or family member could help with driving, and that CR programs could bend to accommodate their schedules and needs.

Discussion. The literature continues to promulgate the benefits of CR at a time when many hospital-based CR programs are closing amid dwindling enrollments. Our study results suggest that organization and personnel dynamics are an important aspect of CR program success. Logistics seemed

relatively less determinant of utilization in programs with optimal organizational dynamics.

At a time when many aspects of medical care are being curtailed, especially if their value is deemed marginal, we assert that hospital-based CR is more impactful and feasible than many may appreciate. However, for patients to take advantage of CR, organizations must implement or reinforce good working relationships between cardiology and CR services and organizational processes that systematize CR referrals. Therefore, rather than dismissing hospital-based CR as impractical, we identified an opportunity to initiate changes that foster an organizational climate favorable to this vital secondary prevention program.

Daniel E. Forman, MD

VA Pittsburgh Healthcare System
Pittsburgh, PA

University of Pittsburgh Medical Center
Pittsburgh, PA

University of Pittsburgh
Pittsburgh, PA

Gemmae M. Fix, PhD

Sarah McDannold, MPH
Edith Nourse Rogers Memorial
Veterans Hospital
Bedford, MA

Boston University School of Public Health
Boston, MA

Nathalie McIntosh, PhD

VA Boston Healthcare System
Boston, MA

David W. Schopfer, MD, MAS

Mary A. Whooley, MD
San Francisco Veterans Affairs Medical Center
San Francisco, CA

University of California
San Francisco, CA

Martin P. Charns, DBA

VA Boston Healthcare System
Boston University School of Public Health
Boston, MA

1. Sandesara PB, Lambert CT, Gordon NF, et al. Cardiac rehabilitation and risk reduction: time to "rebrand and reinvigorate." *J Am Coll Cardiol*. 2015;65(4):389-395.
2. Forman DE. Cardiac rehabilitation: the mandate grows [editorial]. *Mayo Clin Proc*. 2016;91(2):125-128.
3. Drozda J Jr, Messer JV, Spertus J, et al. ACCF/AHA/AMA-PCI 2011 performance measures for adults with coronary artery disease and hypertension: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association—Physician Consortium for Performance Improvement. *J Am Coll Cardiol*. 2011;58(3):316-336.
4. Balady GJ, Ades PA, Bittner VA, et al. Referral, enrollment, and delivery of cardiac rehabilitation/secondary prevention programs at clinical centers and beyond: a presidential advisory from the American Heart Association. *Circulation*. 2011;124(25):2951-2960.
5. Taylor RS, Dalal H, Jolly K, et al. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev*. 2015;8:CD007130.
6. Schopfer DW, Takemoto S, Allsup K, et al. Cardiac rehabilitation use among veterans with ischemic heart disease. *JAMA Intern Med*. 2014;174(10):1687-1689.

<http://dx.doi.org/10.1016/j.mayocp.2016.04.019>

Induction of Atrial Fibrillation by Topical Use of Nasal Decongestants

To the Editor: In recent years, risk factors for atrial fibrillation such as obesity, arterial hypertension, and diabetes have been identified. In this context also, drugs such as β_2 -agonists, bisphosphonates, anabolic steroids, and xanthine derivatives have been claimed to be associated with atrial fibrillation. The following report details the occurrence of atrial fibrillation in association with topical decongestants.

Report of Cases. A 60-year-old woman presented to our outpatient clinic because she had noticed an arrhythmic heartbeat for the preceding 5 days. She reported no continuous medication usage. Electrocardiography revealed atrial fibrillation with a heart rate of 100 beats/min. No abnormalities were noted on echocardiography and laboratory investigations. Electrical cardioversion was performed, and β -blocker therapy was initiated. However, 10 days later, atrial fibrillation recurred. During a second detailed inquiry, the patient reported that she had been using topical decongestants

containing tramazoline for many years to treat recurrent sinusitis. She had severe attacks of congestion despite up to 5 applications of the decongestant per day. She was advised to stop using decongestants immediately and underwent a second electrical cardioversion. After this second cardioversion, the patient has remained without a recurrence for 6 months.

Three weeks after the second cardioversion, the patient's 62-year-old husband came to our outpatient clinic with atrial fibrillation. He also had a history of severe recurrent sinusitis and used decongestants on a regular basis with excessive applications during attacks, similar to his wife. Two months before his visit to our outpatient clinic, pulmonary vein isolation had been performed at another hospital. However, atrial fibrillation recurred 2 weeks after ablation. The husband was also advised to stop using decongestants immediately, and after electrical cardioversion, he has had stable sinus rhythm.

Discussion. Although previous reports have revealed that topical nasal decongestant abuse can cause severe systemic effects such as ischemic stroke,¹ hypertension,² and reversible cardiomyopathy,³ to my knowledge, these patients are the first reported cases indicating that nasal decongestant use can cause atrial fibrillation. Tramazoline is an imidazoline derivative that binds to peripheral α -adrenergic and imidazoline receptors and thereby increases arterial pressure and causes complex neuroendocrine reactions.⁴ These substances are absorbed by mucous membranes, and in pediatric patients, the potentially severe risks of toxicity are well known.⁵

Nasal congestion is a major health problem with an estimated incidence of 30% in the general population. Decongestants cause fast and sustained relief of symptoms. Because they are available without prescription, there is an increased risk of uncontrolled applications taken for longer periods of time

and at higher dosages than recommended. Long-term use can cause rebound congestion leading to rhinitis medicamentosa. Topical application of drugs such as β_2 -agonists prescribed for patients with chronic obstructive pulmonary disease has already been reported to be associated with atrial fibrillation. In this scenario, however, these drugs are taken under medical supervision, whereas a high number of unreported cases of abuse must be estimated for nasal decongestants. The pulmonary vein isolation the husband underwent underlines the lack of awareness of the potential risks of these drugs by patients and doctors.

Heinrich Wieneke, MD

Elisabeth-Krankenhaus-Essen GmbH
Essen, Germany

1. Costantino G, Ceriani E, Sandrone G, Montano N. Ischemic stroke in a man with naphazoline abuse history. *Am J Emerg Med*. 2007;25(8):983.e1-983.e2.
2. Buysschaert I, Van Dorpe J, Dujardin K. Hypertensive crisis and end-organ damage induced by over-the-counter nasal decongestant abuse. *Eur Heart J*. 2011;32(24):3114.
3. Figueiras-Graillet LM, Martínez-Sellés M, Perez-David E, Fernandez-Avilés F. Reversible cardiomyopathy due to chronic use of xylometazoline topical nasal spray. *Int J Cardiol*. 2013;164(2):e17-e18.
4. Peng N, Meng QC, King K, Oparil S, Wyss JM. Acute hypertension increases norepinephrine release in the anterior hypothalamic area. *Hypertension*. 1995;25(4, pt 2):828-833.
5. Tobias JD, Cartabuke R, Taghon T. Oxymetazoline (Afrin®): maybe there is more than we need to know [editorial]. *Paediatr Anaesth*. 2014;24(8):795-798.

<http://dx.doi.org/10.1016/j.mayocp.2016.04.011>

CORRECTION



In the Original Article entitled, "Exercise Capacity and Atrial Fibrillation Risk in Veterans: A Cohort Study" published in the May 2016 issue of *Mayo Clinic Proceedings (Mayo Clin Proc*. 2016;91(5):558-566), Figure 1 was incorrect. The Y axis should be labeled "Event-free Probability," and the legend should read "Probability of not developing atrial fibrillation according to fitness categories."

<http://dx.doi.org/10.1016/j.mayocp.2016.05.005>