

Cochrane for Clinicians

Putting Evidence into Practice

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

A collection of Cochrane for Clinicians published in *AFP* is available at <http://www.aafp.org/afp/cochrane>.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 697. Author disclosure: No relevant financial affiliations.

Self-Monitoring and Self-Management of Oral Anticoagulation

WILLIAM E. CAYLEY JR., MD, MDiv
University of Wisconsin Department of Family Medicine, Eau Claire, Wisconsin

Clinical Question

Does self-monitoring or self-management improve the safety, effectiveness, and feasibility of long-term oral anticoagulation therapy compared with traditional monitoring?

Evidence-Based Answer

In patients taking warfarin (Coumadin) for anticoagulation, there is moderate-quality evidence that both self-monitoring (number needed to treat [NNT] = 100) and self-management (NNT = 53) reduce thromboembolic events, and that self-management reduces all-cause mortality (NNT = 67). There is low- to moderate-quality evidence that neither self-management nor self-monitoring reduces major or minor hemorrhage. Physicians should consider self-management or self-monitoring for patients who are willing and able to use these strategies.¹ (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Portable point-of-care (POC) devices for monitoring long-term oral anticoagulation have been available since the 1990s. Self-monitoring is a strategy in which the patient can measure his or her international normalized ratio (INR) with a POC device, then adjust warfarin dosing by calling a clinic for advice. Self-management strategies refer to patient use of a POC device to measure the INR and adjust warfarin dosage according to a predetermined schedule on physician-approved algorithms. Advantages of both strategies may include patient convenience, ease of monitoring, and fewer thromboembolic complications. A 2006 study suggested that self-monitoring and self-management

are cost-effective strategies for those receiving long-term oral anticoagulation.²

A previous version of this review found that use of POC devices by patients for self-monitoring or self-management of anticoagulation improved all-cause mortality, rates of venous thromboembolism, and rates of minor hemorrhage. Self-monitoring also improved rates of major hemorrhage.³

In updating this Cochrane review, the authors found 10 new trials with 4,227 additional patients to bring the aggregate to 28 randomized controlled trials including 8,950 participants.¹ The authors assessed risk of bias as low to moderate because blinding participants to allocation was not possible. Studies lasted from three months to nearly five years.

Using this larger body of literature, the authors found that when compared with standard care, self-monitoring of anticoagulation reduced thromboembolic events (absolute risk reduction [ARR] = 1%; 95% confidence interval [CI], 0.1% to 1.8%; NNT = 100 [95% CI, 56 to 1,000]), whereas self-management of anticoagulation reduced thromboembolic events (ARR = 1.9%; 95% CI, 1.1% to 2.4%; NNT = 53 [95% CI, 42 to 91]) and all-cause mortality (ARR = 1.5%; 95% CI, 0.5% to 2.1%; NNT = 67 [95% CI, 48 to 200]). The authors also found a greater reduction in thromboembolic events for patients with atrial fibrillation compared with those who had mechanical heart valves and self-monitored or self-managed anticoagulation therapy. The larger evidence base (with the inclusion of the additional studies) no longer shows that self-monitoring reduces all-cause mortality. There is also no evidence that either approach is associated with lower or higher rates of minor or major hemorrhage (*Table 1*).¹

Self-monitoring or self-management may not be feasible for up to one-half of patients needing anticoagulation; barriers encountered by study participants included physical limitations, ability to properly use a monitor, ability to participate in training, and ability

Table 1. Outcomes of Self-Monitoring and Self-Management of Anticoagulation vs. Standard Care

Outcome	Self-monitored anticoagulation	Self-managed anticoagulation
Thromboembolism	Improved	Improved
All-cause mortality	No different	Improved
Major hemorrhage	No different	No different
Minor hemorrhage	No different	No different

Information from reference 1.

to successfully complete training. Furthermore, the evidence to date is insufficient to provide valid comparative information between POC monitors regarding ease of use, accuracy, and patient costs (after insurance coverage).⁴

The findings of this updated review are consistent with previous evidence, as well as a 2012 meta-analysis of individual patient data from 11 studies that found a significant reduction in thromboembolic events in the self-monitoring group, especially among younger patients and those with mechanical heart valves.⁵ A 2015 health technology assessment also had similar overall findings, and noted that costs of self-monitoring and self-management over 10 years were similar to costs of standard monitoring.⁴

For venous thromboembolism, current guidelines recommend warfarin or a direct anticoagulant (e.g., apixaban [Eliquis], dabigatran [Pradaxa], rivaroxaban [Xarelto]).⁶ For many patients with atrial fibrillation, guidelines now recommend using a direct anticoagulant; however, for those with stage IV chronic kidney disease, a mechanical prosthetic valve, or rheumatic mitral stenosis, warfarin is still preferred.⁷ Current guidelines from the U.K.'s National Institute for Health and Care Excellence (NICE) recommend using POC monitors for self-monitoring of anticoagulation by patients with atrial fibrillation or heart valve disease who can be suitably trained,⁸ but NICE does not recommend self-monitoring or self-management for patients with venous thromboembolism.⁹

The practice recommendations in this activity are available at <http://www.cochrane.org/CD003839>.

EDITOR'S NOTE: The numbers needed to treat reported in this Cochrane for Clinicians were calculated by the author based on raw data provided in the original Cochrane review.

REFERENCES

1. Heneghan CJ, Garcia-Alamino JM, Spencer EA, et al. Self-monitoring and self-management of oral anticoagulation. *Cochrane Database Syst Rev.* 2016;(7):CD003839.

- Regier DA, Sunderji R, Lynd LD, Gin K, Marra CA. Cost-effectiveness of self-managed versus physician-managed oral anticoagulation therapy. *CMAJ.* 2006;174(13):1847-1852.
- Garcia-Alamino JM, Ward AM, Alonso-Coello P, et al. Self-monitoring and self-management of oral anticoagulation. *Cochrane Database Syst Rev.* 2010;(4):CD003839.
- Sharma P, Scotland G, Cruickshank M, et al. The clinical effectiveness and cost-effectiveness of point-of-care tests (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system) for the self-monitoring of the coagulation status of people receiving long-term vitamin K antagonist therapy, compared with standard UK practice: systematic review and economic evaluation. *Health Technol Assess.* 2015;19(48):1-172.
- Heneghan C, Ward A, Perera R, et al. Self-monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data [published correction appears in *Lancet.* 2012;379(9821):1102]. *Lancet.* 2012;379(9813):322-334.
- Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines [published correction appears in *Chest.* 2012;142(6):1689-1704]. *Chest.* 2012;141(2 suppl):e419S-e494S.
- You JJ, Singer DE, Howard PA, et al. Antithrombotic therapy for atrial fibrillation: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012;141(2 suppl):e531S-e575S.
- National Institute for Health and Care Excellence. Atrial fibrillation and heart valve disease: self-monitoring coagulation status using point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor). NICE diagnostics guidance [DG14]. September 2014. <http://www.nice.org.uk/guidance/dg14>. Accessed August 30, 2016.
- National Institute for Health and Care Excellence. Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. NICE clinical guideline [CG144]. Updated November 2015. <http://www.nice.org.uk/guidance/CG144>. Accessed August 30, 2016.

Physical Fitness Training for Patients with Stroke

MICHAEL J. ARNOLD, MD

Naval Hospital Jacksonville, Jacksonville, Florida

Clinical Question

Does physical fitness training improve disability after stroke?

Evidence-Based Answer

There is moderate-quality evidence that physical fitness training improves disability after stroke. Cardiovascular training that includes only aerobic exercise has a moderate effect on disability (standard mean difference [SMD] = 0.52 on a pooled disability scale), although it is not clear whether this effect is sustained after patients stop training.¹ (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) There is insufficient evidence to determine whether resistance training has a beneficial effect on disability. Mixed cardiovascular and resistance training has a small effect on disability and is of questionable clinical relevance.¹ (SOR: B, based on inconsistent or limited-

quality patient-oriented evidence.) There is no evidence of reduced risk of stroke recurrence, nor is there risk of harm from physical fitness training in patients after a stroke.¹

Practice Pointers

Stroke is the fifth most common cause of death and a primary cause of adult disability in the United States.² Nearly 3% of U.S. adults are stroke survivors.³ Physical fitness levels in these patients are degraded because of the neurologic effects of stroke, tendency for physical inactivity, and predisposing poor baseline fitness.⁴ Exercise interventions may improve disability and decrease stroke recurrence, but evidence regarding the effect is limited to small trials with diverse functional measures.

This Cochrane review included 58 randomized trials and 2,797 patients.¹ Training sessions were diverse in mode, intensity, duration, and proximity to stroke, limiting comparability of results. Some trials included nonambulatory participants, whereas others included only ambulatory patients. Meta-analysis showed no effect on mortality, independence, or stroke recurrence after physical fitness training.

The best evidence of benefit was found for cardiovascular training. Eight trials showed that cardiovascular training reduced disability at the end of the intervention (SMD = 0.52; 95% confidence interval [CI], 0.19 to 0.84; an SMD greater than 0.5 represents a moderate effect). Measures of mobility were significantly improved, including maximal walking speed (mean difference [MD] = 6.71 meters per minute; 95% CI, 2.73 to 10.69), preferred gait speed (MD = 4.28 meters per minute; 95% CI, 1.71 to 6.84), and walking distance (MD = 30.29 meters in six minutes; 95% CI, 16.19 to 44.39). These mobility effects may have contributed to the disability improvement. Three trials included follow-up assessment at three to six months. There was no evidence of sustained disability improvement; however, some mobility improvements were sustained.

Neither resistance training nor mixed resistance and cardiovascular training conferred the benefits of cardiovascular training alone. There was insufficient

evidence to show that resistance training resulted in a sustained effect on disability. Mixed training reduced disability at the end of the intervention (SMD = 0.26; 95% CI, 0.04 to 0.49; an SMD of 0.2 to 0.5 represents a small effect). However, it is unclear whether this represents a clinically important outcome. Mixed training, which included walking, showed some of the same mobility benefits as cardiovascular training alone, including preferred gait speed (MD = 4.54 meters per minute; 95% CI, 0.95 to 8.14) and walking distance (MD = 41.60 meters in six minutes; 95% CI, 25.25 to 57.95). The actual effect on mobility was uncertain because benefit was demonstrated only if exercise was initiated after usual care.

A previous evidence review that did not include a meta-analysis suggested that exercise interventions benefit patients who have had a stroke.⁵ Guidelines from the U.K.'s National Institute for Health and Care Excellence recommend cardiovascular and resistance exercise training for these patients.⁶

The practice recommendations in this activity are available at <http://www.cochrane.org/CD003316>.

The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the U.S. government.

REFERENCES

1. Saunders DH, Sanderson M, Hayes S, et al. Physical fitness training for stroke patients. *Cochrane Database Syst Rev*. 2016;(3):CD003316.
2. Benjamin EJ, Blaha MJ, Chiuve SE, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2017 update: a report from the American Heart Association [published correction appears in *Circulation*. 2017;135(10):e646]. *Circulation*. 2017;135(10):e146-e603.
3. Schiller JS, Lucas JW, Peregoy JA. Summary health statistics for U.S. adults: National Health Interview Survey, 2011. *Vital Health Stat*. 2012;10(256):1-218.
4. Billinger SA, Coughenour E, Mackay-Lyons MJ, Ivey FM. Reduced cardiorespiratory fitness after stroke: biological consequences and exercise-induced adaptations. *Stroke Res Treat*. 2012;2012:959120.
5. Ivey FM, Macko RF, Ryan AS, Hafer-Macko CE. Cardiovascular health and fitness after stroke. *Top Stroke Rehabil*. 2005;12(1):1-16.
6. National Institute for Health and Care Excellence. Stroke rehabilitation in adults. Clinical guideline CG162. June 2013. <https://www.nice.org.uk/guidance/CG162>. Accessed April 26, 2017. ■