

## REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 9-A-07

Subject: Home Anticoagulation Monitoring  
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Referred to: Reference Committee E  
(Paul C. Matson, MD, Chair)

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1 Resolution 825, introduced by the Indiana Delegation and adopted at the 2005 Interim meeting,  
2 asked that our American Medical Association (AMA) encourage all third-party payers to extend  
3 coverage and reimbursement for home monitors and supplies for home self-monitoring of  
4 anticoagulation for all medically appropriate conditions; and that the issue of home self-monitoring  
5 be referred for further study of problems including, but not limited to: (1) accuracy of equipment and  
6 disposables; (2) willingness and ability of patients to perform both self-testing and quality control as  
7 recommended by equipment manufacturers; (3) correct communication of results to a monitoring  
8 physician; and (4) willingness of a physician in the absence of any funding stream for payment to  
9 assume the responsibility and potential professional liability for overseeing home self-monitoring.

10  
11 This Council report responds to the second resolved of Resolution 825 (I-05) and describes  
12 the scientific evidence with respect to the safety and efficacy of home monitoring of oral  
13 anticoagulation therapy. Much of the data are from Europe where effective payment exists  
14 and use of self-monitoring/management of oral anticoagulation therapy is much more  
15 widespread, particularly Germany and the United Kingdom. In the United States, the  
16 published literature suggests that the main barrier to increased utilization of self-monitoring  
17 and management is the cost of home monitoring equipment and reagents, but other barriers,  
18 such as lack of physician awareness and advocacy, have also been cited. Current AMA  
19 Policy H-185.951 (AMA Policy Database) encourages all third party payers to extend  
20 coverage and reimbursement for home monitors and supplies for home self-monitoring of  
21 anti-coagulation for all medically appropriate conditions. Significantly, review of the  
22 existing evidence suggests that patient self-management of oral anticoagulant therapy is at  
23 least as good as conventional clinical management.

### 24 25 Data Sources

26  
27 Literature searches conducted in the PubMed database for English-language articles published  
28 between 1998 and 2007 using the search term “home anticoagulation” yielded a total of 155  
29 references; 63 articles/reviews directly relevant to the safety and effectiveness of home monitoring of  
30 anticoagulation therapy were selected for further review. An additional 22 references were culled  
31 from the 63 articles selected for further review.

### 32 33 Introduction

34  
35 Over the past decade, indications for the use of oral anticoagulation therapy to reduce the risk of  
36 thromboembolism have increased dramatically.<sup>1-4</sup> Oral anticoagulation therapy began in the 1940s,  
37 after the discovery of dicumerol in 1939.<sup>5</sup> However, discovery in the 1950s of the coumarin

1 derivative warfarin sodium (warfarin) led to the current indications for anticoagulation therapy.<sup>5</sup>  
2 Indeed, warfarin has been the dominant oral anticoagulant for almost 50 years.<sup>6</sup>

3  
4 Oral anticoagulation with vitamin K antagonists, such as warfarin, phenprocoumon, or acenoumarol,  
5 clearly reduces and/or can be used to treat thromboembolic events.<sup>7</sup> It is estimated that well-  
6 controlled anticoagulation with warfarin could prevent more than half the strokes related to atrial  
7 fibrillation and to heart valve replacements.<sup>8</sup> The objective of such treatment is to maintain levels of  
8 anticoagulation capable of preventing thromboembolic events, yet not increase the risk of  
9 hemorrhagic complications.<sup>9</sup> This balancing is necessary due to the variable effects coumarin has on  
10 the hemostatic system that results in significant variations between patients in the dosage required to  
11 achieve therapeutic effect. Also, frequent dosage adjustments are needed for individual patients in  
12 order to maintain a therapeutic level of anticoagulation.<sup>10-13</sup>

13  
14 The international normalized ratio (INR) system was established by the World Health Organization  
15 and the International Committee on Thrombosis and Hemostasis to standardize reporting of results of  
16 blood coagulation (clotting) tests, particularly the prothrombin time (PT) test.<sup>14</sup> The PT test is  
17 performed by adding a patient's plasma to thromboplastin that converts prothrombin to thrombin.  
18 The mixture is then kept in a warm water bath at 37°C for 1 to 2 minutes. Calcium chloride is added  
19 to the mixture to counteract the sodium citrate and allow clotting to proceed. The test is timed from  
20 the addition of the calcium chloride until the plasma clots: this is the prothrombin time. The INR is  
21 the ratio of a patient's prothrombin time to a control sample. With the advent of the INR, clinical  
22 management of anticoagulation therapy improved greatly.<sup>1</sup>

23  
24 The therapeutic range for anticoagulants is narrow; an INR less than 2 increases the risk of  
25 thromboembolism, while an INR greater than 4 to 5 increases the patient's risk of hemorrhage.<sup>15-18</sup>  
26 Accordingly, patients' INR values must be monitored frequently with appropriate adjustment of  
27 anticoagulant dosing to maintain them within this narrow therapeutic range. However, the frequency  
28 of testing is constrained by factors such as the availability of testing facilities, the patient's access to  
29 places where testing can be performed, and the time constraints of the patient and the treating  
30 physician. Unfortunately, because of these barriers, patients are often tested only every 4 to 6 weeks  
31 and consequently may be in a therapeutic range only 40% to 60% of the time.<sup>5</sup>

32  
33 It is apparent that if the frequency of testing could be increased it would yield more accurate INR  
34 data and would, therefore, allow the patient's anticoagulant dosing to be adjusted more frequently to  
35 maintain him or her within a therapeutic range. Indeed, existing data indicate this to be true.<sup>5,7,19,20</sup>  
36 As such, there is strong interest in the use of self-management of anticoagulation therapy in order to  
37 increase the frequency of INR testing and the accompanying adjustment of dosage, if necessary. The  
38 questions that remain are related to issues of safety and efficacy, acceptability, and payment.

39  
40 Importantly, no significant outcomes differences were reported in the literature between self-  
41 monitoring (where the patient tests his/her own INR value and the physician adjusts the  
42 anticoagulant dose) and self-management (where the patients tests his/her own INR value and adjusts  
43 his/her anticoagulant dose independently) and both are therefore treated interchangeably in this  
44 report.

#### 45 46 Safety and Efficacy of Self-Monitoring and Self-Management of Anticoagulation Therapy

##### 47 48 *Systematic Reviews/Meta-analyses*

49  
50 Several systematic reviews have examined the safety and efficacy of home monitoring of  
51 anticoagulant therapy. One review of four randomized trials concluded that self-management is safe,

1 and revealed no difference in oral anticoagulation control between self-managed care and  
2 management by a specialized anticoagulation clinic.<sup>21</sup> Additionally, this review also demonstrated  
3 that in comparison with routine care by general internists, self-managed care was found to be better.  
4 At the same time, self-management could clearly improve treatment-related quality of life. This  
5 observation has also been borne out by other studies.<sup>22,23</sup>

6  
7 Another meta-analysis of 8 randomized, controlled trials comparing self-management with  
8 conventional care showed that with self-management, the difference in time within an appropriate  
9 therapeutic range was, on average, 10% better.<sup>24</sup> The study also showed that while the rate of major  
10 and fatal bleeding was 3.5% per patient-year with conventional management, it was only 2.4% per  
11 patient-year with self-management. Finally, the rate of thrombosis with conventional management  
12 was 3.9% per patient-year versus only 2.7% with self-management.<sup>24</sup>

13  
14 Another systematic review of 14 randomized trials of self-monitoring demonstrated significant  
15 reductions in thromboembolic events, all-cause mortality, and major hemorrhage.<sup>7</sup> Eleven of the 14  
16 trials also reported improvements in the mean proportion of INR values within therapeutic range.  
17 This same review, however, also noted that self-monitoring is not feasible for all patients and that  
18 appropriate patient selection and training are needed. Patients who should be considered include  
19 those who are on long-term anticoagulation therapy, are well-motivated, and have sufficient manual  
20 dexterity.<sup>25</sup> Two US studies (one from 1989<sup>26</sup> and another from 2000<sup>27</sup>) were included in this  
21 review. These US trials demonstrated results similar to the trials performed in the United Kingdom  
22 and Europe; for example, the more recent Beyth study showed that with patient self-monitoring, the  
23 proportion of total treatment time during which the INR value was within the therapeutic range was  
24 almost twice as long as that of the group under conventional management.<sup>27</sup>

#### 25 26 *Randomized Trials*

27  
28 One of the largest randomized clinical trials, comprising more than 600 patients (the SMART trial),  
29 was completed in the United Kingdom and examined as the primary outcome the percentage of time  
30 spent within the therapeutic range of INR.<sup>28</sup> This trial was also the first in the United Kingdom to  
31 assess clinical effectiveness of self-monitoring of anticoagulation therapy versus routine care. No  
32 significant differences were found in the percentage of time in the therapeutic range between self-  
33 managed patients and those under routine care. However, patients who had poor INR control before  
34 SMART showed an improvement in control of INR that was not seen in those undergoing routine  
35 care. There were no significant differences in adverse events between the two arms of the trial.

36  
37 A randomized trial on 733 adults performed in Spain compared self-management of oral  
38 anticoagulant therapy with clinic management and demonstrated that major complications (7.3% of  
39 patients in the conventional management group versus 2.2% in the self-managed group) and minor  
40 hemorrhages (36.4% in the conventional management group versus 14.9% in the self-managed  
41 group) were less common in the self-managed patient group.<sup>1</sup> As with other studies, this report also  
42 demonstrated no inferiority with respect to INR values between those on self-management and those  
43 undergoing conventional clinic management. Similarly, a randomized prospective trial in Germany,  
44 comprising more than 200 patients, also demonstrated that self-management of oral anticoagulation  
45 therapy in patients with atrial fibrillation was not inferior to conventional care.<sup>29</sup> Another trial in  
46 Denmark on 100 patients indicated that when a composite endpoint (combining the variance of INR  
47 value, death, major complications) was examined, the quality of self-managed oral anticoagulation  
48 therapy was comparable to conventional management by a physician or hospital. However, in the  
49 analysis where specific endpoints, such as time within therapeutic INR range, were examined, the  
50 difference favoring patient self-management was statistically higher.<sup>30</sup> A Belgian study involving 66  
51 group practices examined different patient interventions with self-managed anticoagulation therapy.

1 Significantly, the study reiterates the finding that self-management of anticoagulation therapy is  
2 comparable to conventional management.<sup>31</sup>

3  
4 Finally, a large randomized controlled trial is being administered as part of the Veteran Affairs  
5 Cooperative Studies Program to compare anticoagulation therapy managed via frequent patient self-  
6 testing monitored by a home device with high quality management performed by a conventional  
7 anticoagulation service.<sup>32</sup> This study's primary outcome measure is event rates, defined as the  
8 percentage of patients who have a stroke or major bleed or who die. Secondary outcomes also being  
9 examined include total time the INR is in the therapeutic range, competence and compliance with  
10 self-testing, patient satisfaction, quality of life, and cost-effectiveness. The results from this US trial  
11 will further elucidate the role of self-management in anticoagulation therapy.

### 12 *Accuracy of In-home INR Devices*

13  
14  
15 Several studies are now available that validate the use of home-based monitors to evaluate patient  
16 INR values.<sup>33</sup> In general, these devices use freeze-dried thromboplastin reagents packaged in strips  
17 or cuvettes. A drop of fresh blood is applied to a prewarmed reaction chamber, reconstitutes the  
18 thromboplastin, and starts the reaction. The device detects the clotting time, which is then converted  
19 into a plasma prothrombin time equivalent and an INR value by a microprocessor.<sup>5</sup>

20  
21 INR values from Food and Drug Administration (FDA)-approved in-home testing devices correlated  
22 significantly with standard laboratory measurement.<sup>5,34-36</sup> However, there are clear differences in the  
23 quality of devices produced by different manufacturers.<sup>33,37</sup> Thus, it is essential that devices selected  
24 have received FDA approval for prescription in-home use.<sup>5</sup> Additionally, pediatric studies have  
25 confirmed the safety and accuracy of in-home INR monitoring devices.<sup>38,39</sup>

26  
27 Quality assurance studies in Europe demonstrated that the INR values obtained by patients using in-  
28 home devices as compared to values obtained via a laboratory were comparable.<sup>40,41</sup> There was no  
29 statistically significant difference between the mean INR values. However, there is clearly a need to  
30 ensure continued quality of self-monitoring of anticoagulant therapy. For example, monitors should  
31 be recalled periodically for recalibration, devices should include quality control material to be run  
32 every time the instrument is used, and patients should be educated on what to do when control runs  
33 fail.<sup>5</sup> The presence of a comprehensive quality assurance program would make self-monitoring of  
34 anticoagulant therapy even safer and more effective.<sup>5,41</sup>

### 35 Acceptability of Self-Monitoring and Self-Management of Anticoagulation Therapy

36  
37  
38 There is clear patient acceptance of self-monitoring or self-management. One study found a  
39 significant improvement in treatment-related quality of life when patients were on self-managed  
40 anticoagulant therapy versus routine care given by physicians.<sup>22</sup> A study in the Netherlands  
41 observed improved satisfaction with treatment and a decrease in perceived daily distress when  
42 patients were on self-managed therapy.<sup>42</sup> A Danish study indicated that self-management increased  
43 general treatment satisfaction and decreased distress, perceived daily hassles, and strain on the social  
44 network.<sup>43</sup> While a randomized trial performed in Canada failed to show a significant benefit of  
45 patient self-management versus physician management<sup>44</sup>, this study also demonstrated that self-  
46 management was not inferior and, significantly, patients on self-managed therapy preferred to  
47 continue to with this therapy after the trial ended.

48  
49 For patient self-monitoring and management of anticoagulant therapy to be successful, only  
50 appropriate patients should be offered the option. The British Society of Hematology<sup>45</sup> and the  
51 International Self-Monitoring Association for Oral Anticoagulation<sup>25</sup> have published separate but

1 similar guidelines for selecting patients for self-management. Patients under consideration should  
2 meet a number of criteria, including: (1) have indications for long-term anticoagulant therapy, such  
3 as artificial heart valve prosthesis, chronic atrial fibrillation, thrombophilia, and post-myocardial  
4 infarction; (2) be capable and willing to perform self-management; and (3) successfully complete a  
5 structured training course and have demonstrated competence in using the in-home instrument and  
6 interpreting and reporting the results.

7  
8 One critical component of successful self-management of oral anticoagulant therapy is education of  
9 the patient. This component requires not only patient education on the principles of their disease and  
10 the need for monitoring, but also patient training on the technical aspects of performing their own  
11 tests. Patients must also have rudimentary problem-solving skills so they can identify problems and  
12 seek corrective assistance as necessary.<sup>46</sup> Voller and co-workers have demonstrated that application  
13 of a structured training program for patients not only significantly increases patient knowledge of  
14 anticoagulant therapy and home monitoring, but also that the knowledge level remains high without  
15 need for refresher training.<sup>47</sup> Trained patients also experience less fear of complications, and the  
16 limitations on their daily lives are perceived to be less severe. Finally, this study also demonstrated a  
17 high acceptance by patients of the training program.

18  
19 No data exist on the willingness of a physician in the absence of any funding stream for payment to  
20 assume the responsibility and potential professional liability for overseeing home self-monitoring. A  
21 national survey of anticoagulation specialists in the United States indicated that most believed self-  
22 monitoring of anticoagulant therapy would increase in this country if cost barriers were overcome.  
23 These barriers include the cost of the self-testing devices and of the reagents.<sup>48</sup>

#### 24 25 Payment Issues Related to Self-Monitoring and Self-Management of Anticoagulation Therapy

26  
27 In general, while initial costs for beginning in-home self management are high, when the length of  
28 long-term anticoagulant therapy coupled with increased medical benefits and improved patient  
29 quality of life are factored in, self-management is usually cost-effective. The few studies that have  
30 examined the cost-effectiveness of self-managed anticoagulant therapy versus conventional  
31 management are from Europe and the United Kingdom, and generally demonstrate the intervention  
32 to be either cost-effective or cost-saving.

33  
34 A German study showed a 50% cost savings with self-management as compared to routine care, but  
35 the only costs considered were those covered by government health insurance.<sup>49</sup> A Canadian study  
36 compared the costs and quality-adjusted life years accrued to patients self-managing their  
37 anticoagulant therapy compared to those receiving physician management, and showed the average  
38 discounted incremental cost of self-management over physician management to be CA\$989 per  
39 patient, suggesting that self-management is a cost-effective strategy for those receiving long-term  
40 therapy.<sup>44</sup> A Belgian randomized controlled trial compared patient self-monitoring with an in-home  
41 device with conventional management and determined that implementation of a combination of  
42 multifaceted education with use of the in-home INR measuring device is a cost-effective model for  
43 oral anticoagulation management.<sup>50</sup>

44  
45 On the other hand, two studies from the United Kingdom did not demonstrate cost-effectiveness of  
46 self-management of oral anticoagulant therapy.<sup>51,52</sup> In both of these trials the investigators  
47 emphasized that their conclusions are relative to the cost-effectiveness criteria of the UK health  
48 system. In both studies the authors also concede that other factors such as the ability of self-  
49 management to reduce the burden on outpatient facilities, clinician time, and time of amortization of  
50 the INR device were not accounted for.

1 Finally, in homebound elderly patients taking warfarin in the United States, anticoagulation  
 2 monitoring using a portable INR device was shown to be cost-saving.<sup>53</sup> Another study in 2000  
 3 concluded that when the costs incurred by provider organizations and patients are considered, patient  
 4 self-testing is more cost-effective than routine care or care at an anticoagulation clinic and resulted in  
 5 an overall cost saving.<sup>54</sup>

6  
 7 More data on the cost-effectiveness of patient self-management of anticoagulant therapy are needed<sup>55</sup>  
 8 to improve payment for self-management interventions in the United States. In 2002, Medicare  
 9 began covering the cost of weekly home-based INR monitoring for patients with mechanical heart  
 10 valves.<sup>5</sup> The scientific findings detailed above provide important evidence to support improved  
 11 payment for self-management of anticoagulant therapy by Medicare and other insurers for patients  
 12 with other indications for long-term anticoagulation therapy.

13  
 14 Guidelines for Implementing Patient Self-testing and Management of Anticoagulant Therapy

15  
 16 At least two guidelines exist on the implementation of patient self-management of anticoagulant  
 17 therapy. These guidelines, from the British Society of Hematology<sup>45</sup> and the International Self-  
 18 Monitoring Association for Oral Anticoagulation,<sup>25</sup> provide clear criteria for consideration, including  
 19 patient selection criteria, patient training and education, quality assurance, and frequency of  
 20 monitoring.

21  
 22 Conclusions

23  
 24 There are few United States-specific randomized controlled studies with respect to patient self-  
 25 management of oral anticoagulant therapy. However, the few US data that exist support the more  
 26 substantial body of evidence from the United Kingdom, Europe, and Australia that patient self-  
 27 management is safe and effective. Appropriate selection and training of patients is necessary, and  
 28 there are at least two existing guidances on the appropriate use of home monitoring. Additionally,  
 29 patients appear to have improved quality of life and to prefer self-monitoring over conventional  
 30 techniques. Cost-effectiveness data are limited and need to be improved, but existing data suggest  
 31 that self-management of anticoagulation therapy is minimally cost-effective and potentially cost-  
 32 saving. However, at the present time such data are highly country- and health system-specific.

33  
 34 RECOMMENDATIONS

35  
 36 The Council on Science and Public Health recommends that the following statements be adopted,  
 37 and that the remainder of this report be filed:

- 38  
 39 1. That our American Medical Association (AMA) support the appropriate use of home self-  
 40 monitoring of oral anticoagulation therapy. (New HOD Policy)  
 41  
 42 2. That our AMA continue to monitor safety and effectiveness data, in particular cost-  
 43 effectiveness data, specific to the United States on home management of oral anticoagulation  
 44 therapy. (Directive to Take Action)  
 45  
 46 3. That our AMA reaffirm existing Policy H-185.951, Home Anti-Coagulation Monitoring.  
 47 (Reaffirm HOD Policy)

Fiscal Note: \$750

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