Guidelines for implementation of patient self-testing and patient self-management of oral anticoagulation.

International consensus guidelines prepared by International Self-Monitoring Association for Oral Anticoagulation

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Abstract

\textbf{Aims:} This document provides health care professionals involved in initiating and monitoring oral anticoagulation therapy with guidelines for the provision of safe and effective patient self-testing/patient self-management of oral anticoagulation.

\textbf{Methods and results:} The consensus group has critically reviewed the literature and compared the results of usual care (UC) vs. anticoagulation clinic and patient self-management/patient self-testing (PSM/PST). The education and training of patients for self-monitoring are described, together with the suitability of patients, the effect on quality of life and cost-effectiveness.

The consensus agrees that patient self-testing and patient self-management are effective methods of monitoring oral anticoagulation therapy, providing outcomes at least as good as, and possibly better than, those achieved with an anticoagulation clinic. All patients must be appropriately selected and trained.

Currently available self-testing/self-management devices give INR results which are comparable with those obtained in laboratory testing. The most frequent testing frequency is weekly but lower frequency of testing can be justified based on institutional or patient conditions.

\textbf{Conclusions:} The consensus agrees that there are several points in favour of PST/PSM, for example, a higher degree of medical safety, increased patient education, improved response to changes in lifestyle, increased independence for the patient and improved quality of life. © 2004 Elsevier Ireland Ltd. All rights reserved.

Keywords: Patient self-management; Oral anticoagulant therapy; International Normalised Ratio; Coagulometer; International consensus guidelines

1. Introduction

Oral anticoagulation with coumarin derivatives is prescribed to a steadily increasing number of patients as lifelong therapy for indications such as mechanical heart valves, atrial fibrillation or inherited/acquired thrombophilic disorders. In addition, oral anticoagulation therapy has been shown to effectively prevent arterial embolism in a wide variety of clinical conditions \cite{1–3}.

The ability to maintain patients within a desired therapeutic range required for oral anticoagulation therapy is a challenge due to two main factors. These are the narrow pharmacologic therapeutic range of the coumarin derivatives, and the variability of their biological effect \cite{4}. This variable dose response results in difficulties in initial dose selection and stabilisation, as well as long-term difficulties in maintaining stability.

It has been shown that improved anticoagulant control results in improved outcomes, with a decrease in the incidence of bleeding complications and thromboembolic events \cite{5}. It is, therefore, essential to maintain close control of the intensity of anticoagulation in order to minimise the
adverse thrombotic and haemorrhagic events which occur with under- and over-anticoagulation [6].

Patient self-testing (PST) and patient self-management (PSM) of oral anticoagulation potentially offer further advantages over other approaches. PST is when a patient determines his/her own INR, with dose regulation by the physician; PSM is when the patient is responsible for INR determination and for dose adjustment within given limits, as demonstrated by Cosmi et al. [7].

PST and PSM are not new modalities in chronically ill patients. Regular metabolic monitoring and adjustment of the insulin dose and diabetic diet are accepted worldwide in well-trained diabetic patients and are indispensable parts of diabetic therapy. Patients on long-term oral anticoagulant therapy now also have the option of PST/PSM. There are currently over 100,000 patients performing PST/PSM of oral anticoagulation in Germany alone and a significant amount of information has been collected from these patients over the last few years.

This document has been prepared in order to provide health care professionals involved in initiating and monitoring oral anticoagulation therapy with guidelines for the provision of safe and effective Patient self-testing/self-management of oral anticoagulation. This consensus has been derived from the results of published clinical studies in selected groups of patients, together with extensive experience in clinical practice. It has been developed and agreed upon by specialists with considerable experience in this field as being the best current practice in terms of PST and PSM.

2. Usual care vs. anticoagulation clinic care vs. patient self-testing/self-management

Most patients receiving chronic oral anticoagulation today are managed by their own physician, along with all other patients in their physician’s practice. There is no organised programme of management, education or follow-up. Only a few studies have specifically assessed clinical outcomes in this ‘usual care (UC)’ model of management (Table 1) [8–11]. These studies indicate a rate of major haemorrhage of at least 7–8% per patient year of therapy. There is a similar rate of recurrent or de novo thromboembolism with an overall serious adverse event rate of at least 15% per patient year of therapy. These adverse events are generally a consequence of poor therapeutic control, with haemorrhage or thrombosis

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### Table 1
Frequency of major haemorrhage/thromboembolism in patients managed under a usual care model of management

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Number of patient years</th>
<th>Years of data collection</th>
<th>New or established patients</th>
<th>Indications</th>
<th>Major haemorrhage (%)</th>
<th>Fatal haemorrhage (%)</th>
<th>Rec TE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beyth [10]</td>
<td>264</td>
<td>440</td>
<td>1986–1993</td>
<td>New</td>
<td>Ven &amp; art</td>
<td>5.0</td>
<td>0.68</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>1772</td>
<td>2293</td>
<td></td>
<td></td>
<td></td>
<td>6.6</td>
<td>0.9</td>
<td>8.1</td>
</tr>
</tbody>
</table>

NA = not available; Rec TE = recent thromboembolism; haem = haemorrhage.

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### Table 2
Frequency of major haemorrhage/thromboembolism in patients managed under an anticoagulation management service

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Number of patient years</th>
<th>Years of data collection</th>
<th>New or established patients</th>
<th>Indications</th>
<th>Target PTR/INR</th>
<th>Major haemorrhage (%)</th>
<th>Fatal haemorrhage (%)</th>
<th>Rec TE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conte [14]</td>
<td>140</td>
<td>153</td>
<td>1975–1984</td>
<td>N&amp;E</td>
<td>Ven &amp; art</td>
<td>1.7–2.5PTR</td>
<td>2.6</td>
<td>NA</td>
<td>8.4</td>
</tr>
<tr>
<td>Petty [15]</td>
<td>310</td>
<td>385</td>
<td>1977–1980</td>
<td>N&amp;E</td>
<td>Ven &amp; art</td>
<td>1.5–2.5PTR</td>
<td>0.0</td>
<td>0.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Charney [16]</td>
<td>73</td>
<td>77</td>
<td>1981–1984</td>
<td>N&amp;E</td>
<td>Ven &amp; art</td>
<td>1.5–2.0PTR</td>
<td>0.0</td>
<td>0.0</td>
<td>NA</td>
</tr>
<tr>
<td>Bussey [17]</td>
<td>82</td>
<td>199</td>
<td>1977–1986</td>
<td>N</td>
<td>Ven &amp; art</td>
<td>1.5–2.0PTR</td>
<td>3.8</td>
<td>0.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Seabrook [18]</td>
<td>93</td>
<td>158</td>
<td>1981–1988</td>
<td>N</td>
<td>Ven &amp; art</td>
<td>1.5–2.0PTR</td>
<td>0.0</td>
<td>0.0</td>
<td>NA</td>
</tr>
<tr>
<td>Fihm [19]</td>
<td>928</td>
<td>1950</td>
<td>NA</td>
<td>N</td>
<td>Ven &amp; art</td>
<td>1.3–1.5PTR</td>
<td>1.7</td>
<td>0.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Van der Meer [20]</td>
<td>6814</td>
<td>6085</td>
<td>1988</td>
<td>N&amp;E</td>
<td>Ven &amp; art</td>
<td>2.4–3.5INR</td>
<td>3.3</td>
<td>0.64</td>
<td>NA</td>
</tr>
<tr>
<td>Cannegieter [21]</td>
<td>1609</td>
<td>6475</td>
<td>1985–1993</td>
<td>N&amp;E</td>
<td>Mech valves</td>
<td>3.6–4.8INR</td>
<td>2.5</td>
<td>0.33</td>
<td>0.7</td>
</tr>
<tr>
<td>Total</td>
<td>13,475</td>
<td>18,960</td>
<td></td>
<td></td>
<td></td>
<td>2.8</td>
<td>0.39</td>
<td>2.6</td>
<td></td>
</tr>
</tbody>
</table>

NA = not available; Rec TE = recent thromboembolism; PTR = prothrombin time ratio; INR = International Normalised Ratio; haem = haemorrhage.

* Major and fatal haemorrhage and thromboembolism rates expressed as percent per patient year of therapy; fatal haemorrhagic events also included with major haemorrhage.

b Ven and art = mixed indications in the venous and arterial system.
occurring as a consequence of excessive or subtherapeutic anticoagulation.

A co-ordinated and focused approach to the management of therapy by specialised programmes (anticoagulation clinic care, ACC) significantly improves clinical outcomes by improving therapeutic control and time-in-therapeutic range (TTR), lessening the frequency of haemorrhage or thrombosis and decreasing the use of medical resources.

Table 3
Frequency of major haemorrhage/thromboembolism in patients managed under usual medical care vs. anticoagulation management service

<table>
<thead>
<tr>
<th>Study</th>
<th>Model of care</th>
<th>Number of patients</th>
<th>Number of patient years</th>
<th>Years of data collection</th>
<th>Indications</th>
<th>Target PTR/INR</th>
<th>Maj haem&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Fatal haem&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Rec TE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garabedian-Ruffalo [24]</td>
<td>UC</td>
<td>26</td>
<td>64.3</td>
<td>177–1980</td>
<td>Ven &amp; art&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.5–2.5&lt;sup&gt;PTR&lt;/sup&gt;</td>
<td>12.4</td>
<td>0</td>
<td>6.2</td>
</tr>
<tr>
<td></td>
<td>AMS</td>
<td>26</td>
<td>41.9</td>
<td>1980–1983</td>
<td>Ven &amp; art</td>
<td>1.5–2.5&lt;sup&gt;PTR&lt;/sup&gt;</td>
<td>2.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cortelazzo [25]</td>
<td>UC</td>
<td>271</td>
<td>677</td>
<td>1982–</td>
<td>Mech valves</td>
<td>25–35%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4.7</td>
<td>0</td>
<td>6.6</td>
</tr>
<tr>
<td></td>
<td>AMS</td>
<td>271</td>
<td>669</td>
<td>1987–1990</td>
<td>Mech valves</td>
<td>3.0–4.5&lt;sup&gt;INR&lt;/sup&gt;</td>
<td>1.0</td>
<td>0</td>
<td>0.6</td>
</tr>
<tr>
<td>Wilt [26]</td>
<td>UC</td>
<td>44</td>
<td>28</td>
<td>1988–1993</td>
<td>Ven &amp; art</td>
<td>NA</td>
<td>17.8</td>
<td>0</td>
<td>42.8</td>
</tr>
<tr>
<td></td>
<td>AMS</td>
<td>68</td>
<td>60</td>
<td>1988–1993</td>
<td>Ven &amp; art</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chiquette [27]</td>
<td>AMS</td>
<td>82</td>
<td>199</td>
<td>1977–1986</td>
<td>Ven &amp; art</td>
<td>NA</td>
<td>2.0</td>
<td>NA</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>UC</td>
<td>142</td>
<td>102</td>
<td>1991–1992</td>
<td>Ven &amp; art</td>
<td>NA</td>
<td>3.9</td>
<td>0.9</td>
<td>11.8&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>AMS</td>
<td>176</td>
<td>123</td>
<td>1992–1994</td>
<td>Ven &amp; art</td>
<td>NA</td>
<td>1.6</td>
<td>0</td>
<td>3.3</td>
</tr>
</tbody>
</table>

UC = usual care; AMS = anticoagulation management service; TE = thromboembolism; PTR = prothrombin time ratio; INR = International Normalised Ratio.

<sup>a</sup> Major and fatal haemorrhage, thromboembolism, and cost savings rates expressed as percent per patient year of therapy; fatal haemorrhagic events included with major haemorrhage.

<sup>b</sup> Ven and art = mixed indications in the venous and arterial systems.

<sup>c</sup> Prothrombin activity.

<sup>d</sup> Two TE events fatal.

Table 4
Capillary whole blood (point-of-care) PT instruments

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Clot detection methodology</th>
<th>Type of sample</th>
<th>Home use approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protime Monitor 1000</td>
<td>Clot initiation: Thromboplastin</td>
<td>Capillary WB</td>
<td>No</td>
</tr>
<tr>
<td>Coumatra&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Clot detection: Cessation of blood flow through capillary channel</td>
<td>Venous WB</td>
<td></td>
</tr>
<tr>
<td>Ciba Corning 512 Coagulation Monitor&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoaguChek Plus&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoaguChek Pro&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoaguChek Pro/DM&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoaguChek</td>
<td>Clot initiation: Thromboplastin</td>
<td>Capillary WB</td>
<td>Yes&lt;sup&gt;b&lt;/sup&gt; (not yet submitted for approval in the USA)</td>
</tr>
<tr>
<td>CoaguChek S</td>
<td>Clot detection: Cessation of movement of iron particles</td>
<td>Venous WB</td>
<td></td>
</tr>
<tr>
<td>Thrombolytic Assessment System Rapidpoint Coag</td>
<td>Clot initiation: Thromboplastin</td>
<td>Capillary WB</td>
<td>Yes</td>
</tr>
<tr>
<td>ProTIME Monitor</td>
<td>Clot detection: Cessation of blood flow through capillary channel</td>
<td>Venous WB</td>
<td></td>
</tr>
<tr>
<td>Hemochron Jr&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEM PCL&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Clot initiation: Thromboplastin</td>
<td>Capillary WB</td>
<td>Yes</td>
</tr>
<tr>
<td>Avosure Pro&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Clot detection: Thrombin generations detected by fluorescent thrombin probe</td>
<td>Venous WB</td>
<td></td>
</tr>
<tr>
<td>Avosure Pro&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avosure PT&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harmony</td>
<td>Clot initiation: Thromboplastin</td>
<td>Capillary WB</td>
<td>Yes</td>
</tr>
<tr>
<td>INRatio&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Clot detection: Cessation of blood flow through capillary channel</td>
<td>Venous WB</td>
<td>Approved</td>
</tr>
<tr>
<td></td>
<td>Clot detection: Change in impedance in sample</td>
<td>Capillary WB</td>
<td></td>
</tr>
</tbody>
</table>

WB = whole blood.

<sup>a</sup> All instruments in this category are based on the original Biotrack model (Protime Monitor 1000) and licensed under different names. The latest version available is the CoaguChek Pro and Pro/DM (as models evolved they acquired added capabilities); earlier models no longer available.

<sup>b</sup> CoaguChek not actively marketed for home use at the time of this writing. Thrombolytic Assessment System not available for home use.

<sup>c</sup> Hemochron Jr and GEM PCL are simplified version of the ProTIME Monitor.

<sup>d</sup> Avosure instruments removed from market when manufacturer (Avocet) ceased operations (2001). Technology has since been purchased by Beckman-Coulter.

<sup>e</sup> INRatio, manufactured by Hemosense, gained Self Test FDA approval in the US in November 2002 and has since received the Self-Test CE mark.
leading to more cost-effective therapy. These positive outcomes from ACC have been demonstrated in a large number of retrospective, and some prospective, studies of care delivered by an anticoagulation clinic (Table 2) [12–23]. These mostly observational studies indicate a greater than 50% reduction in both major haemorrhage and thrombosis compared to UC.

Lastly, Table 3 summarises studies examining both models of management where co-ordinated care is measured against a control group of UC [24–27]. These mostly non-randomised, retrospective analyses provide further evidence for the benefit of co-ordinated care.

3. Patient self-testing and patient self-management

There is potential for further simplifying and improving anticoagulation management by point-of-care (POC) testing. Since the late 1980s, several devices have been introduced or are in development (Table 4) [28].

These instruments are based on clot detection methodology using thromboplastin to initiate clot formation, while the end-point of clot detection varies from instrument to instrument. Although limitations of these instruments have been described, POC instruments have been tested in a number of different clinical settings and their accuracy and precision are considered to be more than adequate for the monitoring of oral anticoagulant therapy [29] in both adults and children [30–35].

Studies comparing clinical outcomes (either TTR or adverse events) have shown a marked difference between PSM and UC. Other similar comparisons have shown outcomes at least as good as, and possibly better than, those achieved with ACC. Table 5 summarises those studies where clinical outcomes, either TTR or adverse events, have been reported [36–49].

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Study groups</th>
<th>Number of patients</th>
<th>Time in range (%/pt-yr)</th>
<th>Maj haem (% or days)</th>
<th>TE (%/pt-yr)</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beyth [36]</td>
<td>RCT</td>
<td>PST</td>
<td>162</td>
<td>56</td>
<td>5.7</td>
<td>9</td>
<td>Mixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC</td>
<td>163</td>
<td>33</td>
<td>12</td>
<td>13</td>
<td>Mixed</td>
</tr>
<tr>
<td>Horstkotte [37]</td>
<td>RCT</td>
<td>PSM</td>
<td>75</td>
<td>92</td>
<td>4.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.9</td>
<td>Heart valves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC</td>
<td>75</td>
<td>59</td>
<td>10.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.6</td>
<td>Heart valves</td>
</tr>
<tr>
<td>Sawickij [38]</td>
<td>RCT</td>
<td>PSM</td>
<td>90</td>
<td>57/53&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.2</td>
<td>2.2</td>
<td>Mixed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC</td>
<td>89</td>
<td>34/43&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.2</td>
<td>4.5</td>
<td>Mixed</td>
</tr>
<tr>
<td>Hasenkam [39]</td>
<td>Obs</td>
<td>PSM</td>
<td>20</td>
<td>77</td>
<td>NA</td>
<td>NA</td>
<td>Heart valves</td>
</tr>
<tr>
<td></td>
<td>Matched cont</td>
<td>UC</td>
<td>20</td>
<td>53</td>
<td>NA</td>
<td>NA</td>
<td>Heart valves</td>
</tr>
<tr>
<td>Körkke [40]</td>
<td>RCT</td>
<td>PSM</td>
<td>305</td>
<td>78</td>
<td>1.7</td>
<td>1.2</td>
<td>Heart valves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC</td>
<td>295</td>
<td>61</td>
<td>2.6</td>
<td>2.1</td>
<td>Heart valves</td>
</tr>
<tr>
<td>White [41]</td>
<td>RCT</td>
<td>PST</td>
<td>23</td>
<td>93</td>
<td>0</td>
<td>0</td>
<td>Mixed</td>
</tr>
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<td></td>
<td></td>
<td>ACC</td>
<td>23</td>
<td>75</td>
<td>0</td>
<td>0</td>
<td>Mixed</td>
</tr>
<tr>
<td>Kaatz [42]</td>
<td>RCT</td>
<td>PST</td>
<td>NA</td>
<td>63</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ACC</td>
<td>NA</td>
<td>65</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ansell [43]</td>
<td>Obs</td>
<td>PSM</td>
<td>20</td>
<td>89</td>
<td>0</td>
<td>0</td>
<td>Mixed</td>
</tr>
<tr>
<td></td>
<td>Matched cont</td>
<td>ACC</td>
<td>20</td>
<td>68</td>
<td>0</td>
<td>0</td>
<td>Mixed</td>
</tr>
<tr>
<td>Watzke [44]</td>
<td>Prospective</td>
<td>PSM</td>
<td>49</td>
<td>86</td>
<td>4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>Mixed</td>
</tr>
<tr>
<td></td>
<td>Controlled</td>
<td>ACC</td>
<td>53</td>
<td>80</td>
<td>0</td>
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<tr>
<td>Cromheecke [45]</td>
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<td>50</td>
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<tr>
<td></td>
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<td>49</td>
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<tr>
<td>Gadisseur [46]</td>
<td>Cross-over</td>
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<td>28</td>
<td>70</td>
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<tr>
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<td>RCT</td>
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<td>23</td>
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<tr>
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<td>68</td>
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<tr>
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<td>Obs</td>
<td>PSM Mixed</td>
<td>1375</td>
<td>69</td>
<td>1.61</td>
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<tr>
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<td>Prospective</td>
<td>PSM</td>
<td>355</td>
<td>73.5</td>
<td>3.28</td>
<td>3.28</td>
<td>Heart valves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC</td>
<td>62.5</td>
<td>4.67</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bernardo [49]</td>
<td>Prospective</td>
<td>PSM</td>
<td>92</td>
<td>83.1</td>
<td>3.38</td>
<td>3.38</td>
<td>Heart valves</td>
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RCT = randomised controlled trial; Obs = observational; PST = patient self-testing; PSM = patient self-management; ACC = anticoagulation clinic; UC = usual care; Mixed = mixed indications. TE = thromboembolic, haem = haemorrhage, maj = major, pt = patient; yr = year.

Note: Both PST and PSM studies are included. The studies are grouped according to whether the comparator arm was a UC model of therapy or an anticoagulation management service. It should be noted that the difference between groups for TTR was considerably less marked when compared to an anticoagulation management service vs. UC.

<sup>a</sup> Major and minor bleeding.

<sup>b</sup> Time in range at 3 and 6 months.

<sup>c</sup> % of episodes in 49 pts.
None of these PST/PSM studies were adequately designed to clearly answer the important question of what might account for better therapeutic control. The major variables not adequately controlled included the level of patient education, the subtle impact on compliance, the frequency of monitoring and the consistency of reagent and instrumentation. Further studies are needed to define the importance of these parameters.

A strong relationship between TTR and bleeding rates has been observed across a large number of studies with different patient populations, different target ranges, different scales for measuring intensity of anticoagulation (i.e. PT, PT ratio and INR) and different models of dosage management [5,17,21,25,26]. A similar relationship holds for TTR and rates of thromboembolism. Many studies indicate that an increased frequency of testing leads to more results within the therapeutic range [31,50]. The frequency of testing is dependant on many factors including patient stability, compliance, fluctuations in co-morbid conditions, the addition or discontinuation of other medications, changes in diet, the quality of dose-adjustment decisions and the stage of treatment [6]. The increased frequency of monitoring of the INR may be a factor for improved outcomes with PST/PSM.

Recently, a German study [48,51] with over 2800 patients followed for a total of 8061 follow-up years after mechanical heart valve replacement suggested that significant fluctuations in consecutive INR measurements were the strongest predictors for both thromboembolic and bleeding events rather than over or under anticoagulation.

Other factors may, however, also be important in this regard. For example, patient education regarding anticoagulation therapy and patient empowerment are important elements in improving quality of treatment and patient awareness and could also be a major factor for improving patient compliance.

Based on the above factors, POC PT monitors offer the potential to lower the risk/benefit profile of anticoagulant therapy, improve patient satisfaction and possibly improve patient compliance. By reducing the labour intensity of physician management, PST/PSM can also encourage more widespread use of oral anticoagulants.

4. Quality of life

As well as improving TTR and reducing the number of potential complications associated with oral anticoagulant therapy, improvement in quality of life is an important benefit which has been observed with PSM [38,45,52].

5. Cost-effectiveness

It has been shown that PSM can be cost-effective in the longer-term. While the initial costs of PSM are higher than those for laboratory monitoring of INR due to the cost of training and providing the coagulation monitor and test strips, several studies [53–55] suggest that PSM is the most cost-effective method of monitoring patients on oral anticoagulation therapy. In a GELIA sub-study [56], the reduction in costs associated with the 30% reduction in severe complications and the 20% reduction in lethal strokes due to bleeding observed with PSM was 52,000 Euro per life year gained. However, it must be noted that cost savings may differ between various countries and different institutions, depending on the costs of the actual system of anticoagulant control.

6. Suitable patients

Patient self-testing/self-management should be considered in patients who are on long-term oral anticoagulation with artificial heart valve prosthesis, chronic atrial fibrillation, thrombophilia (e.g. after recurrent deep vein thrombosis in the leg and pulmonary embolism) and post-myocardial infarction with impaired left ventricular pump function, including advanced congestive cardiomyopathy.

Various studies have found that, as with self-testing and self-management of insulin-dependant diabetes, most patients who are able to lead an independent and Self-supporting life are, in principle, capable of self-testing/self-management of oral anticoagulation, irrespective of education and social status [45,57]. The only requirement in terms of intellectual ability is that the patient (or care giver) is able to understand the concept of oral anticoagulant therapy and its potential risks. Otherwise, the only necessity is willingness to actively participate in treatment, sufficient manual dexterity and acuity of vision. No previous experience in PST/PSM is necessary.

All patients wanting to perform PST/PSM must successfully complete a structured training course and must be willing to accept the responsibility for self-management. The ability to learn how to perform self-management is not associated with a defined age group. However, both age and co-morbidity also play an important role in this decision [58]. If patients are not in a position to perform PST/PSM themselves, care givers, parents [35,59] or other relatives can undertake it on their behalf. Medical supervision of the patient must be continued by regular consultation with the training centre or physician, even when treatment is free from complications.

7. Suitable coagulometers

The coagulometers currently available differ in their physical methods of measurement and in their degree of automation (Table 4). Easy, portable, fully automated coagulation monitors have now become available which allow the reliable determination of the PT, expressed as INR, from one drop of capillary whole blood from a fingerstick [28].
Specific devices shall not be reviewed in these guidelines due to the variations in devices available in different countries. It is sufficient to say that all of the devices that are authorised in each market will have had their accuracy and reliability demonstrated. There are quality assurance programmes available that indicate whether measured INR values are within the recommended consensus values, with numerous coagulometers having been included in these quality assessment programmes (e.g. UK NEQAS).

Issues of reimbursement for devices and test strips must be addressed independently in each country and cannot be addressed within the scope of this document.

8. Education and training

Education on the theoretical and pharmaceutical aspects of anticoagulation is a fundamental requirement for all patients on anticoagulant therapy; training on point-of-care INR testing is essential for those patients in PST/PSM.

Education and training infrastructures will develop differently in each country, depending on local circumstances. However, it will require the development of resources to train the trainers, as well as the patients.

9. Training the trainers

In order that patient training can be successfully achieved, health care professionals who train patients must themselves be trained in the management of anticoagulant therapy and have practical knowledge of PST/PSM devices. There is a considerable amount of comprehensive material already available for trainers. This material should be used as a model wherever possible since relevant standards have already been set and training courses evaluated in clinical practice (e.g. ASA booklet).

Training can be performed successfully by a ‘train-the-trainer’ approach by suitably qualified staff under the supervision of a physician. The training programme for trainers set out by the Anticoagulation Self-management Association (ASA) consists of a 1-day seminar. This covers the theoretical and pharmaceutical aspects of anticoagulation, use of equipment and a practical session. Trainers are then qualified to lead patients through the structured teaching and self-management programme (SPOG) which comprises three lessons of 90–120 min each [32].

Training centres should be open for queries at pre-specified times and it is ideal if 24-h contact details are given to patients in case of emergency. One to three-monthly records of INR values should be monitored by the training centre or the treating physician.

In addition to the ‘train-the-trainer’ approach, trials in the US have demonstrated that carefully structured training programmes that do not follow a ‘train-the-trainer’ approach but teach health care professionals directly have also proven successful.

10. Training the patients

Providing an appropriate education programme is an important part of PST/PSM.

For self-testing, the main goal of training is to teach patients practical skills which enable them to achieve accurate INR results. This must include operation of the monitoring device and finger-pricking technique. For self-management, the main goal is for patients to be able to report INR data, as well as clinical observations regarding their oral anticoagulant therapy, to their health care provider. Furthermore, patients should be able to respond appropriately to required dosage changes. Therefore, PST requires a more sophisticated patient training programme.

The contents of the ASA/SPOG training course include:

- basic information on blood coagulation;
- theoretical principles of individual anticoagulation/drug interactions with oral anticoagulants;
- practical information on coagulation monitoring with coagulometers;
- evaluation of measurements and, if necessary, dose adjustment;
- signs of bleeding events (overdose) and thromboembolic events (underdose);
- information on the frequency of INR determination;
- keeping a patient diary/quality control record keeping;
- travel, nutrition, endocarditis prophylaxis, intramuscular injections, etc.

All training sessions should be concluded with a formalised test which serves to document each patient’s understanding of oral anticoagulant therapy and PST/PSM. Having passed the test, patient should receive a certificate and their performance should be monitored by regular update sessions.

German experience demonstrates efficient, cost-effective training with a patient group size of 3–5 [60] with additional interaction and reinforcement between patients. However, group sizes must be determined by national/local, social and medical traditions.

11. Monitoring of PST/PSM

Despite the ability of patients to self-test/self-manage, adequate clinical support remains essential. On-going education, advice in cases of sustained lack of anticoagulation control and advice on interruption of therapy in cases of bleeding or the need to undergo an invasive procedure are, amongst others, all issues which must be considered. The
anticoagulation clinic can play an important role in over-
seeing such organisation.

To provide a methodical guarantee of the reliability of
PST/PSM, coagulometers should be assessed by training
centres at least once a year. Alternatively, patient devices
can be double-checked with a POC device in the physician’s
office, clinic or laboratory. This offers the added benefit of
monitoring patient handling and ensuring that patient data is
stored in the meter instantly.

12. Summary of consensus

A significant number of patients undergoing lifelong oral
anticoagulation therapy are eligible for PST/PSM. After
structured training by trained health care professionals,
suitable patients are in a position to determine their anti-
coagulation intensity accurately and reliably and selected
patients are also able to adjust their dosages accordingly.

Recent technical developments have produced high-pre-
cision, user-friendly coagulometers. Patients are able to
achieve a stable anticoagulant level with weekly testing,
or more frequently if required, thereby significantly reduc-
ing the number of complications.

PSM may be more cost-effective than usual care or anti-
coagulant clinic care and, above all, considerably improves
quality of life by giving the patient more independence.

Summary of ISMAA recommendations:

- Patient self-testing/self-management is an effective
  method of monitoring oral anticoagulation therapy,
  providing outcomes at least as good as, and possibly
  better than, those achieved with an anticoagulation clinic.
- Available self-testing/self-management devices give INR
  results which are comparable with those obtained in
  laboratory testing.
- The most frequent testing frequency is weekly but lower
  frequency of testing can be justified based on institu-
tional or patient conditions.
- Patients must be appropriately selected and trained.
- Patient self-testing/self-management is the most patient
friendly method for long-term, high frequency monitor-
ing of oral anticoagulation.

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