

CURRENT CLINICAL PRACTICE

Patient understanding of warfarin therapy: A review of education strategies

FIONA NEWALL^{1,2}, PAUL MONAGLE^{1,3}, & LINDA JOHNSTON^{2,4,5}

¹Department of Haematology, Royal Children's Hospital, Flemington Road, Parkville 3052, Vic., Australia, ²School of Nursing, The University of Melbourne, Grattan Street, Carlton 3053, Australia, ³Department of Paediatrics, The University of Melbourne, Grattan Street, Carlton 3053, Australia, ⁴Murdoch Childrens Research Institute, Flemington Road, Parkville 3052, Vic., Australia, and ⁵Department of Neonatology, Royal Children's Hospital, Flemington Road, Parkville 3052, Vic., Australia

(Received 17 June 2005; accepted 5 July 2005)

Abstract

Significant research has been directed into defining best-practice anticoagulant management of thromboembolic events and optimal strategies for determining the safety and efficacy of therapy. Similarly, improved patient outcomes have been realised through the development of novel management strategies such as self-monitoring and self-management. Considerably, less energy has been directed towards developing and evaluating the best mechanisms for delivery of patient education. This is in spite of the fact that numerous confounders to stable therapy confront warfarinised patients on a daily basis. That patients requiring warfarin therapy should be educated with respect to that therapy has never been questioned. However, relatively little attention appears to have been paid to the development of robust models of patient education in the setting of oral anticoagulant therapy. This paper reviews the current literature with respect to warfarin education interventions before recommending strategies that may facilitate determination of the impact educating patients about warfarin therapy has upon clinical outcomes.

Keywords: Warfarin, patient education, education design, knowledge outcomes, anticoagulant control

Introduction

The level of knowledge the patient and family have regarding warfarin therapy is reported to be indirectly proportional to their risk of complications, primarily major bleeding [1,2]. Educational programs that inform families of techniques to reduce bleeding risk are of significant importance. The risk of bleeding due to warfarin therapy is closely related to the adequacy of warfarin control [3–6]. The control of warfarin therapy has been shown to improve in patients who have received written and verbal warfarin education [2,5,7,8]. More food and drug interactions have been reported for warfarin than for any other prescription medication [9]. Understanding these interactions can improve warfarin control [10].

Historically, strategies employed by health professionals to educate patients about their health varied widely and were rarely evaluated [11]. Educational

interventions that take a multidisciplinary approach and are implemented “face-to-face” are reportedly associated with greatest success [12,13]. Clinicians likely invest significant time and energy towards patient education. However, rarely does anyone assess whether such educational interventions actually achieve their desired outcome.

This review aims to critique published education interventions aimed at increasing patient understanding of warfarin therapy. Recommendations will be made with respect to future directions that may improve the efficacy of warfarin education delivery to patients.

Methods

A search of published literature was conducted using the *Medline* search engine, between 1966 and 2004.

Correspondence: F. Newall, Department of Haematology, Royal Children's Hospital, Flemington Road, Parkville 3052, Vic., Australia.

Key terms used to guide the search included: warfarin, patient education, patient teaching, warfarin education, patient knowledge, education, education program and oral anticoagulation and anticoagulant therapy. The search was limited to humans and the English language. The bibliographies of all articles identified were reviewed in an attempt to optimise identification and retrieval of relevant material.

Publications referring to “warfarin education” were identified. All papers were classified according to their educational content. Publications that did not report the implementation of an education intervention were excluded from further analysis.

Education interventions targeting patients requiring warfarin therapy were reviewed with respect to their process of development, use of educational principles or models and the outcome of the intervention. For the purpose of this review, *educational interventions* were categorised as being “structured”, “semi-structured” or “unstructured”. Structured programs adhered to a regimented program that was uniformly implemented by a select individual or small group of individuals. Semi-structured programs were those not uniformly implemented or conducted according to a pre-determined time-frame, were not staffed by individuals specifically assigned to such a role but did incorporate a checklist of educational objectives. Unstructured programs were those that did not possess any characteristics that would ensure the consistent communication of knowledge to participants.

Results

One hundred and ten papers were identified from the *Medline* search. Fifty-three papers referring to the concept of warfarin education but that did not provide any further details were excluded from further analysis. Papers that reported checklists of key topics for warfarin education ($n = 28$) [5,10,14–34] and papers that reported patient knowledge outcomes not within the context of an education intervention ($n = 6$) [33–38] were also excluded from further analysis. Seventeen papers reported studies that incorporated an educational intervention aimed at improving patient understanding of warfarin therapy [2,4,39–53]. In seven of these publications, this intervention was one part of a broader study, with one paper investigating the impact of patient knowledge on compliance with therapy [41], and six papers reporting the implementation of warfarin self-management programs [2,4,40,42,45,47].

Ten publications reported the outcomes of a structured educational intervention, employing a regimented program implemented by selected individuals [2,4,39,42,43,45,48–50,53]. Some form of randomisation to various clinical management strategies was common to six of these papers [2,4,39,43,45,49]. Whilst sixty percent of structured

educational interventions clearly stated the learning objectives of their intervention [2,39,43,45,49,53], only one paper reported patient knowledge outcomes with respect to predetermined stated learning objectives [53].

Determination of post-intervention patient understanding was conducted in 70% of the structured interventions [39,42,43,48–50,52,53]. Three of these seven papers reported baseline knowledge assessments to facilitate determination of improvement in the level of patient understanding post-intervention [48–50]. Two papers reported that participants demonstrated improved understanding of key warfarin-related issues [48,50], with one paper reporting a significant increase in global warfarin knowledge after completion of the intervention [49]. However, one of these baseline knowledge assessments was conducted *after* the patients had participated in the educational intervention, raising significant questions regarding the impact of recall bias on participants’ baseline knowledge [48].

Five papers reported educational interventions that were not uniformly implemented or conducted according to a pre-determined time-frame [41,44,46,51,52]. Semi-structured interventions were most commonly delivered by registered nurses and/or pharmacists. Two papers reporting semi-structured interventions clearly stated their learning objectives [46,52], however, only one of these reported patient knowledge outcomes with respect to predetermined objectives [52]. Wilson et al. was the only paper in this category to report any knowledge-specific outcomes related to their education intervention [52].

Two publications did not possess any characteristics that would ensure the consistent communication of key principles to participants [40,47]. Neither of these papers stated their programs’ learning objectives or assessed participants’ knowledge following the education intervention.

Several approaches to providing warfarin-specific education were identified within the reviewed publications. Rankin and Clark used *programmed instruction* as the foundation for their education interventions [39,43]. Programmed instruction is said to be characterised by a written, logically sequential program that guides the learner through the educational content at their own pace [39,43]. Both authors found that patients requiring warfarin therapy who were educated using programmed instruction achieved a statistically significantly higher score on their global warfarin knowledge assessment compared to their respective control groups [39,43]. Furthermore, Rankin found that retention of warfarin knowledge was greater amongst participants in the programmed instruction arm [43].

Beyth et al. report a multi-component study aimed at reducing the rate of bleeding complications in a

population of older patients. One component of this study was a patient education program grounded in social learning theory and experimental evidence [2]. This approach maintains that patient education alone does not improve clinical outcome but that participation in one's own care can achieve such improvement. This study's endpoints included major bleeding events, death and recurrent thrombosis, but not patient knowledge outcomes. The authors of this paper concluded that their multi-component intervention (inclusive of patient education) was associated with improved outcomes as measured by major bleeding rates. They acknowledge that the study did not assess the individual components of the study and specifically whether this model of education contributed to improved patient outcomes. The ability of interventions grounded in social learning theory and experimental evidence to improve patient understanding of warfarin therapy remains unknown.

The *Predisposing, Reinforcing and Enabling Causes in Educational Diagnosis and Evaluation (PRECEDE)* model of health education was used as the foundation to Wyness' warfarin education intervention [53]. This model acknowledges that success of an education intervention depends upon more than simply identifying the desired outcome (i.e. increasing knowledge). The model facilitates the design, development and evaluation of a robust educational intervention. In this report, patients who received warfarin education based upon the PRECEDE model understood more about their warfarin therapy than patients educated via an unstructured model [53].

Stone et al. found that patients who received warfarin education via a videotape presentation achieved similar knowledge outcomes to patients educated "face-to-face" and that the former was associated with significantly less teaching time [49]. This study randomised patients to receive warfarin education via a video presentation prepared specifically for this study or through the conventional means of a face-to-face encounter. All participants were provided with a question time at the end of their presentations. This study suggests that "face-to-face" educational interventions are not associated with improved knowledge outcomes but its conclusions are limited by its sample size ($n = 22$) which limits the generalisability of its findings. Singla et al. report that group-based warfarin education sessions can improve patient understanding of warfarin therapy, reduce personnel time directed to patient education and are preferred by patients [48]. However, her conclusions are significantly limited by the retrospective assessment of patients' baseline warfarin understanding and the lack of control group comparisons.

None of the publications that incorporated educational interventions into studies investigating a primary intervention *other than* patient knowledge reported any discrete knowledge outcomes of their

study. These publications report their findings with the assumption that provision of an education intervention is associated with improved patient understanding.

Several important limitations were identified amongst papers reporting outcomes of education interventions aimed at improving patients' understanding of warfarin therapy. Most frequently identified, was the lack of baseline knowledge assessments to facilitate determination of a program's success. When assessment occurred, there was poor uniformity of patient knowledge assessments, with key knowledge outcomes such as understanding of confounders to stable therapy largely overlooked. Where knowledge was shown to improve following an intervention, only two publications reported whether that improved level of understanding was retained over time. Finally, no publication has proven a direct causal link between improving patient knowledge of warfarin therapy and improvement in warfarin-related outcomes.

Discussion

A considerable investment of time, finances and energy has been directed to optimising the outcomes of patients requiring oral anticoagulant therapy, particularly over the last two decades [54]. Clinicians are now more knowledgeable about optimal treatment intensity and duration, and have been able to improve the quality of life in patients requiring oral anticoagulant therapy through the development and evaluation of self-monitoring and management programs. Despite these advances, comparatively little effort has been directed towards optimising the process of educating patients about their oral anticoagulant therapy. This paper reviewed the medical literature pertaining to warfarin education in an effort to identify strategies that may improve our ability to adequately educate patients about their anticoagulant therapy.

The Seventh American College of Chest Physicians (ACCP) Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines recommend the incorporation of patient education into the systematic management of patients requiring oral anticoagulant therapy [55]. This recommendation supports the widespread assumption that teaching patients about warfarin will be associated with an improvement in warfarin-related outcomes [1,2,5,7,8,10]. However, practices regarding the provision of that education vary widely with the majority of programs being implemented without consideration to process design. Programs are rarely evaluated with respect to the outcomes of the education process and for most there is no evidence of any association with improved warfarin-related outcomes.

This review assessed published warfarin education interventions according to the level of structure the programs incorporated. Structured programs

[2,4,39,42,43,45,48–50,53] incorporated steps to ensure a systemic approach to education and were more likely to report the outcomes of their intervention than semi-structured [52] or unstructured programs [40,47]. Patients who were educated using strategies based upon established models of education (programmed instruction [39,43], PRECEDE [53]) did appear to achieve improved levels of knowledge than patients educated using unstructured programs. However, as less than 25% of papers reviewed presented education outcomes against measures of baseline understanding, it is not possible to conclude which approach to patient education achieved the best *improvement* in patient knowledge. Educational interventions may be delivered with the best of intentions yet fail to incorporate the structural planning to ensure that interventions are delivered consistently. Several authors have challenged the likelihood of such interventions ever achieving their desired outcome [11,56,57], suggesting structured plans are required.

Two of the papers reviewed explored mechanisms by which warfarin education can be delivered in a more time-efficient manner [48,49]. Stone's conclusion that patient understanding of warfarin therapy did not vary according to whether they were educated via video-tape or face-to-face interventions [49] contradicts that reported by studies investigating outcomes of Asthma education. Education programs aimed at improving patient understanding of asthma invariably take a multidisciplinary approach to patient education and yield greatest success when interventions are made "face-to-face" [12,13]. These findings support Beyth's premise of developing an educational intervention based upon social learning theory which enables the patient to be an active participant in their care, rather than a passive observer [2]. To that end, the group education sessions proposed by Singla [48] require further investigation as they may well facilitate the provision of face-to-face, structured educational interventions that are associated with improved time efficiency.

This paper reviewed all articles published between 1966 and 2004 that were identified through a *Medline* search relating to "warfarin education". All effort was made to include relevant search terms in the *Medline* query, and the bibliographies of all identified articles were reviewed to maximise completeness. However, this review may have excluded some articles relating to warfarin education that were not within the parameters of the database search terms used. It is therefore, possible that a warfarin educational program that has been systematically developed and evaluated is currently being utilised, but was not identified by this review.

The findings of this report lend themselves to two recommendations for practice and one recommendation for future research. First, this review suggests that educational processes aimed at increasing

patients' understanding of warfarin therapy should be assessed to determine whether they are actually achieving their goal of increasing patient understanding of warfarin therapy. Second, the use of educational interventions based upon established models of education may have greater success in achieving their objectives than those that don't. Any service seeking to develop or review a program for educating patients about oral anticoagulant therapy should not only consider the content of the program, but also the process of program development and implementation.

The relationship between adverse event rates and objective measures of patient knowledge has not been confirmed to date and requires further research. There is a generalised acceptance in the medical literature that patients who have a good understanding of warfarin therapy will experience fewer complications with therapy [12]. Given the number of factors that can confound stable anticoagulant therapy, it is logical to conclude that if patients are more knowledgeable about their therapy they will be more stable. However, the relationship between knowledge and frequency of complications needs to be confirmed to justify the resources devoted to warfarin education.

The development and conduct of robust research aimed at improving our understanding of oral anticoagulant therapy has facilitated the development of clinical guidelines that are truly evidence-based [54,58–61]. This level of robust investigation does not appear to have transferred into the domain of patient education, with the majority of interventions reported not adequately assessing whether their warfarin education initiatives are actually improving patient understanding. There is evidence to suggest that the design of the educational intervention is likely to impact upon the effectiveness of any intervention [11]. To date, such evidence appears to have been largely overlooked with respect to the development and implementation of warfarin education programs. Only once the knowledge outcomes of structured educational interventions have been established will it be possible to objectively confirm the effect of increased patient knowledge on factors such as stability of therapy, frequency of adverse events and compliance with management strategies.

References

- [1] Gallus A, Baker R, Chong B, Ockelford P, Street A. Consensus guidelines for warfarin therapy. *Med J Aust* 2000;172:600–605.
- [2] Beyth R, Quinn L, Landefeld C. A multicomponent intervention to prevent major bleeding complications in older patients receiving warfarin: A randomized, controlled trial. *Ann Int Med* 2000;133(9):687–695.
- [3] Ansell J. Oral anticoagulant therapy—50 years later. *Arch Int Med* 1993;305:586–597.
- [4] Cromheecke M, Levi M, Colly L, de Mol B, Prins M, Hutten B, et al. Oral anticoagulation self-management and manage-

- ment by a specialist anticoagulation clinic: A randomised cross-over comparison. *Lancet* 2000;356:97–102.
- [5] Errichetti A, Holden A, Ansell J. Management of oral anticoagulant therapy: Experience with an anticoagulation clinic. *Arch Int Med* 1984;144:1966–1968.
 - [6] Kumar S, Haigh J, Rhodes L, Peaker S, Davies J, Roberts B, et al. Poor compliance is a major factor in unstable outpatient control of anticoagulant therapy. *Thromb Haemost* 1989;62(2):729–732.
 - [7] Paulson P, Bauch R, Lamont Paulson M, Zilz D. Medication data sheets—an aid to patient education. *Drug Intell Clin Pharm* 1976;10:448–453.
 - [8] Horton J, Bushwick B. Warfarin therapy: Evolving strategies in anticoagulation. *Am Family Phys* 1999;59(3):635–646.
 - [9] Heck A, DeWitt B, Lukes A. Potential interactions between alternative therapies and warfarin. *Am J Health-System Pharm* 2000;57:1221–1227.
 - [10] Gibbar-Clements T, Shirrell D, Dooley R, Smiley B. The challenge of warfarin therapy. *Am J Nursing* 2000;100(3):38–40.
 - [11] Wyness M. Warfarin patient education: Are we neglecting the program design process? *Patient Edu Counsel* 1989; 14:159–169.
 - [12] Guendelman S, Meade K, Benson M, Chen Y, Samuels S. Improving asthma outcomes and self-management behaviors of inner-city children: A randomized trial of the health buddy interactive device and an asthma diary. *Arch Pediatr Adolesc Med* 2002;156(2):114–120.
 - [13] Liu C, Feekery C. Can asthma education improve clinical outcomes?. An evaluation of a pediatric asthma education program. *J Asthma* 2001;38(3):269–278.
 - [14] Hickman K, Tortorici M, Knight J. How we operate a useful interdisciplinary teaching program for warfarin patients. *Pharm Times* 1980;3:60–64.
 - [15] Ansell J, Holden A, Nozzolillo D. Oral anticoagulant therapy: Practical considerations. *Nurse Pract Forum* 1992; 3(2):105–113.
 - [16] Erban S. Initiation of warfarin therapy: Recommendations and clinical pearls. *J Thromb Thrombolysis* 1999;7(2):145–148.
 - [17] Fitzmaurice DA, Machin SJ. Recommendations for patients undertaking self management of oral anticoagulation. *BMJ* 2001;323(7319):985–989.
 - [18] Jaffer A, Bragg L. Practical tips for warfarin dosing and monitoring. *Cleveland Clin J Med* 2003;70(4):361–370.
 - [19] Kornblit P, Senderoff J, Davis-Ericksen M, Zenk J. Anticoagulation therapy: Patient management and evaluation of an outpatient clinic. *Nurse Pract* 1990;15(8):21–32.
 - [20] Malacaria B, Feloney C. Going with the flow of anticoagulant therapy. *Nursing* 2003;33(3):36–43.
 - [21] McPherson M, Grace K. Anticoagulant therapy: What to consider in practical management. *Adv Nurse Pract* 1997;32–39.
 - [22] Moore K, Maschak B. How patient education can reduce the risks of anticoagulation. *Nursing* 1977;24–29.
 - [23] Neafsey P. Of blood, bones, and broccoli: Warfarin-Vitamin K interactions. *Home Healthcare Nurse* 2004;22(3):178–182.
 - [24] Oertel L. Monitoring warfarin therapy. *Nursing* 1999; 29(11):41–44.
 - [25] Porter P. The role of the advanced practice nurse in anticoagulation. *AACN Clin Issues* 2002;13(2):221–233.
 - [26] Sheehan O, Stinson J, Feely J. Establishing a primary care based anticoagulation clinic. *Irish Med J* 2000;93(2):45–48.
 - [27] Sidhu P, MacGowan S. Self-managed anticoagulation is safe and effective. *Eur J Cardio-Thoracic Surg* 2003;24:668.
 - [28] Wenger N. Managing ambulatory anticoagulation. *J Thromb Thrombolysis* 2001;12(1):S31–S34.
 - [29] Stuart T. Home monitoring and management of warfarin therapy: An anticoagulation clinic perspective. *J Thromb Thrombolysis* 2000;10(1):55–57.
 - [30] Shapiro R. Anticoagulant therapy. *Am J Nursing* 1974;74(3): 439–443.
 - [31] Coughlin P, Murtagh J. Warfarin anticoagulation. *Aust Family Phys* 1992;21(7):1009–1010.
 - [32] Vogel E. Anticoagulation with warfarin: A review of monitoring issues. *Adv Nurse Pract* 2001;9(1):75–78, 81,94.
 - [33] Swithers C. Tools for teaching about anticoagulants. *RN* 1988; January:57–58.
 - [34] Catania U. Monitoring Coumadin therapy. *RN* 1994; 57(2):29–34.
 - [35] Brigden M. Oral anticoagulant therapy: Practical aspects of management. *Postgrad Med* 1996;99(6):93–94, 100–1001.
 - [36] Barcellona D, Contu P, Sorano G, Pengo V, Marongiu F. The management of oral anticoagulant therapy: The patient's point of view. *Thromb Haemost* 2000;83:49–53.
 - [37] Heller R, Knapp J, Lim L, Carruthers A, Fluit J, O'Connell R, et al. Effectiveness of anticoagulation among patients discharged from hospital on warfarin. *Med J Aust* 1998;169: 243–246.
 - [38] Hennessy B, Vyas M, Duncan B, Allard S. Evaluation of an alternative model of anticoagulant care. *Irish Med J* 2000;169(1):34–36.
 - [39] Clark C, Bayley E. Evaluation of the use of programmed instruction for patients maintained on warfarin therapy. *Am J Public Health* 1972;62(8):1135–1139.
 - [40] Gadisseur A, Breukink-Engbers W, van der Meer F, van den Besselaar AM, Rosendaal F. Comparison of the quality of oral anticoagulant therapy through patient self-management by specialized anticoagulation clinics in the Netherlands. *Arch Int Med* 2003;163(21):2639–2646.
 - [41] Laporte S, Quenet S, Buchmuller-Cordier A, Reynaud J, Tardy-Poncet B, Thirion C, et al. Compliance and stability of INR of two oral anticoagulants with different half-lives: A randomised trial. *Thromb Haemost* 2003;89:458–467.
 - [42] Morsdorf S, Erdlenbruch W, Taborski U, Schenk J, Erdlenbruch K, Novotny-Reichert G, et al. Training patients for self-management of oral anticoagulant therapy: Standards, patient suitability, and clinical aspects. *Semin Thromb Hemost* 1999;25(1):109–115.
 - [43] Rankin M. Programmed instruction as a patient teaching tool: A study of myocardial infarction patients receiving warfarin. *Heart Lung* 1979;8(3):511–516.
 - [44] Refsum N. Counselling patients on oral anticoagulant therapy—a pilot study. *J Clin Pharm Therap* 1987; 12:173–179.
 - [45] Sawicki P. A structured teaching and self-management program for patients receiving oral anticoagulation. *JAMA* 1999;281(2):145–150.
 - [46] Scalley R, Kearney E, Jakobs E. Interdisciplinary inpatient warfarin education program. *Am J Hospital Pharm* 1979; 36:219–220.
 - [47] Sidhu P, O'Kane H. Self-managed anticoagulation: Results from a two-year prospective randomized trial with heart valve patients. *Ann Thorac Surg* 2001;72:1523–1527.
 - [48] Singla D, Jasser G, Wilson R. Effects of group education on patient knowledge, knowledge gained, and cost-efficiency in an anticoagulation centre. *J Am Pharmaceut Assoc* 2003;43(2):264–266.
 - [49] Stone S, Holden A, Knapic N, Ansell J. Comparison between videotape and personalized patient education for anticoagulant therapy. *J Family Pract* 1989;29(1):55–57.
 - [50] Taylor F, Ramsay M, Renton A, Cohen H. Patients' knowledge of warfarin treatment. *Quality Health Care* 1994;3:230.
 - [51] Waterman A, Milligan P, Banet G, Gatchel S, Gage B. Establishing and running an effective telephone-based anticoagulation service. *J Vasc Nursing* 2001;19(4):126–133.
 - [52] Wilson F, Racine E, Tekieli V, Williams B. Literacy, readability and cultural barriers: Critical factors to consider when educating older African Americans about anticoagulation therapy. *J Clin Nursing* 2003;12:275–282.

- [53] Wyness M. Evaluation of an educational programme for patients taking warfarin. *J Adv Nursing* 1990;15:1052–1063.
- [54] Hirsh J, Bates SM. Clinical trials that have influenced the treatment of venous thromboembolism: A historical perspective. *Ann Int Med* 2001;134(5):409–417.
- [55] Ansell J, Hirsh J, Poller L, Bussey H, Jacobson A, Hylek E. The pharmacology and management of the Vitamin K antagonists. *Chest* 2004;126(3 Suppl):204S–233S.
- [56] Edelman C, Mandle C. Health promotion throughout the lifespan. 3rd ed. St Louis: Mosby; 1994.
- [57] Hawe P, Degeling D, Hall J. Evaluating health promotion: A health worker's guide. 1st ed. Sydney: MacLennan and Petty; 1992.
- [58] Hull R, Delmore B, Genton E, Hirsh J, Gent M, Sackett D, et al. Warfarin sodium versus low-dose heparin in the long-term treatment of venous thrombosis. *N Engl J Med* 1979;301:855–858.
- [59] Hull R, Hirsh J, Jay R, Carter C, England C, Gent M, et al. Different intensities of oral anticoagulant therapy in the treatment of proximal vein thrombosis. *N Engl J Med* 1982;307:1676–1681.
- [60] Kearon C, Gent M, Hirsh J, Weits J, Kovacs M, Anderson D, et al. A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. *N Engl J Med* 1999;340:901–907.
- [61] Schulman S, Rhedin A, Lindmarker P, Carlsson A, Larfars G, Nicol P, et al. A comparison of six weeks with six months of oral anticoagulant therapy after a first episode of idiopathic venous thromboembolism. Duration of anticoagulation trial study group. *N Engl J Med* 1995;332:1661–1665.