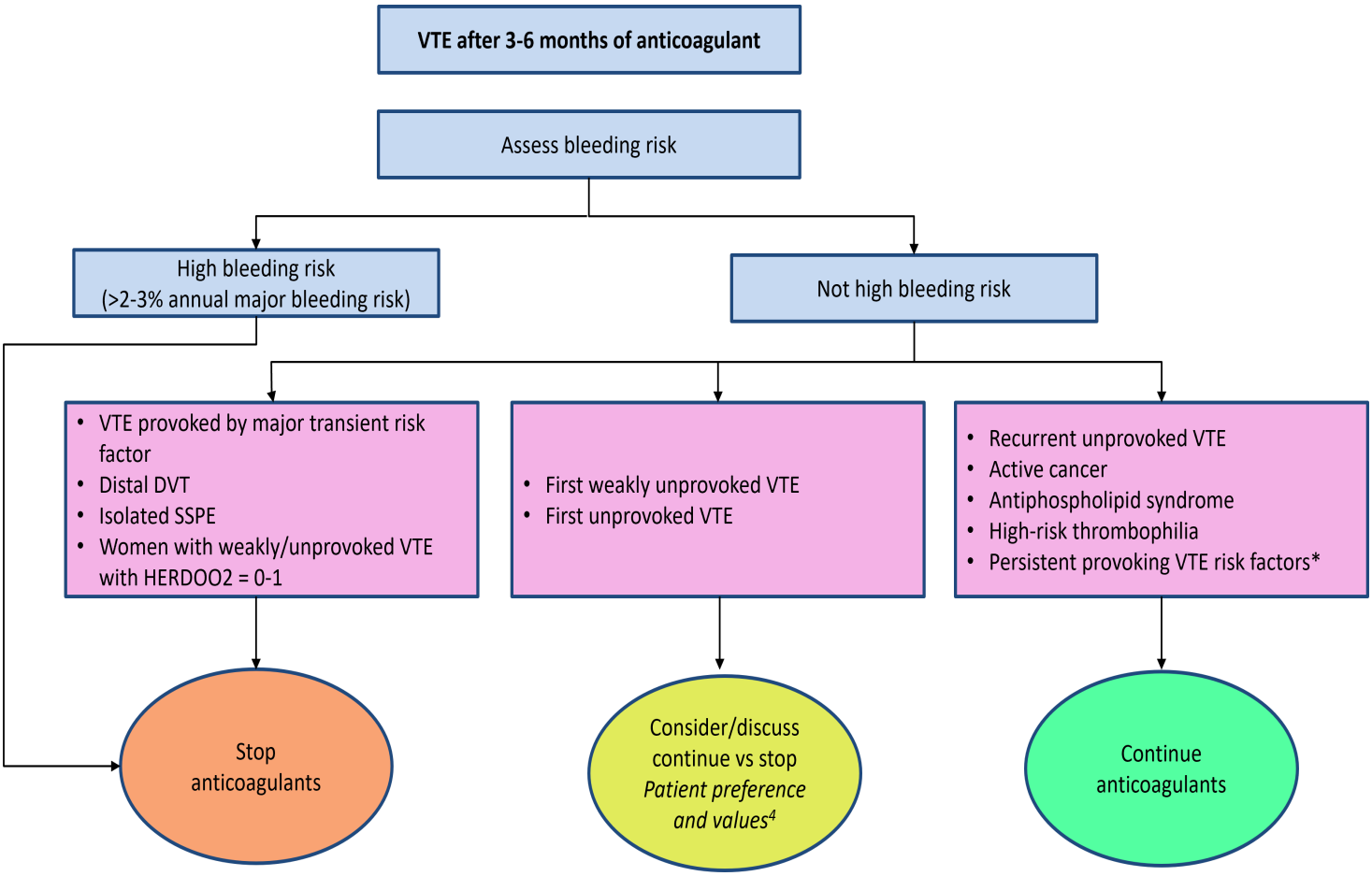
Venous Thromboembolism: Duration of Treatment

Thrombosis Canada
Thrombose Canada

Key Takeaways

Patients with strongly provoked VTE, women with low HERDOO2 scores, patients with subsegmental pulmonary embolism (SSPE), patients with distal deep vein thrombosis (DVT) or patients with a high bleeding risk should stop anticoagulants (Figure 1). Patients with cancer-associated VTE should continue anticoagulants while cancer is active. In the remaining patients with weakly provoked or unprovoked VTE, extending anticoagulant therapy does not confer a meaningful net mortality or quality of life benefit but reduces the substantial risk of recurrent VTE. In weakly/unprovoked VTE scenarios, patients and providers must engage in shared decision-making, weighting the risk and consequences of recurrent VTE against the risks, burdens and preferences associated with continuing anticoagulants.

Figure 1. Continue or stop anticoagulants after initial 3-6 months of treatment for acute VTE



*Persistent provoking VTE risk factors: Ongoing immobility, obesity (BMI ≥30), heart failure, chronic lung disease, chronic kidney disease (eGFR <60), chronic inflammatory/autoimmune disease or chronic infection. Patients with atherosclerotic cardiovascular disease should continue ASA.
†Preference-sensitive "tie zone": First weakly provoked or first unprovoked VTE. Shared decision-making is required.
If continuing, prefer reduced-dose DOAC (apixaban 2.5 mg BID or rivaroxaban 10 mg OD).

Objective:

To provide updated, evidence-based guidance on the recommended duration of anticoagulant therapy for venous thromboembolism (VTE).

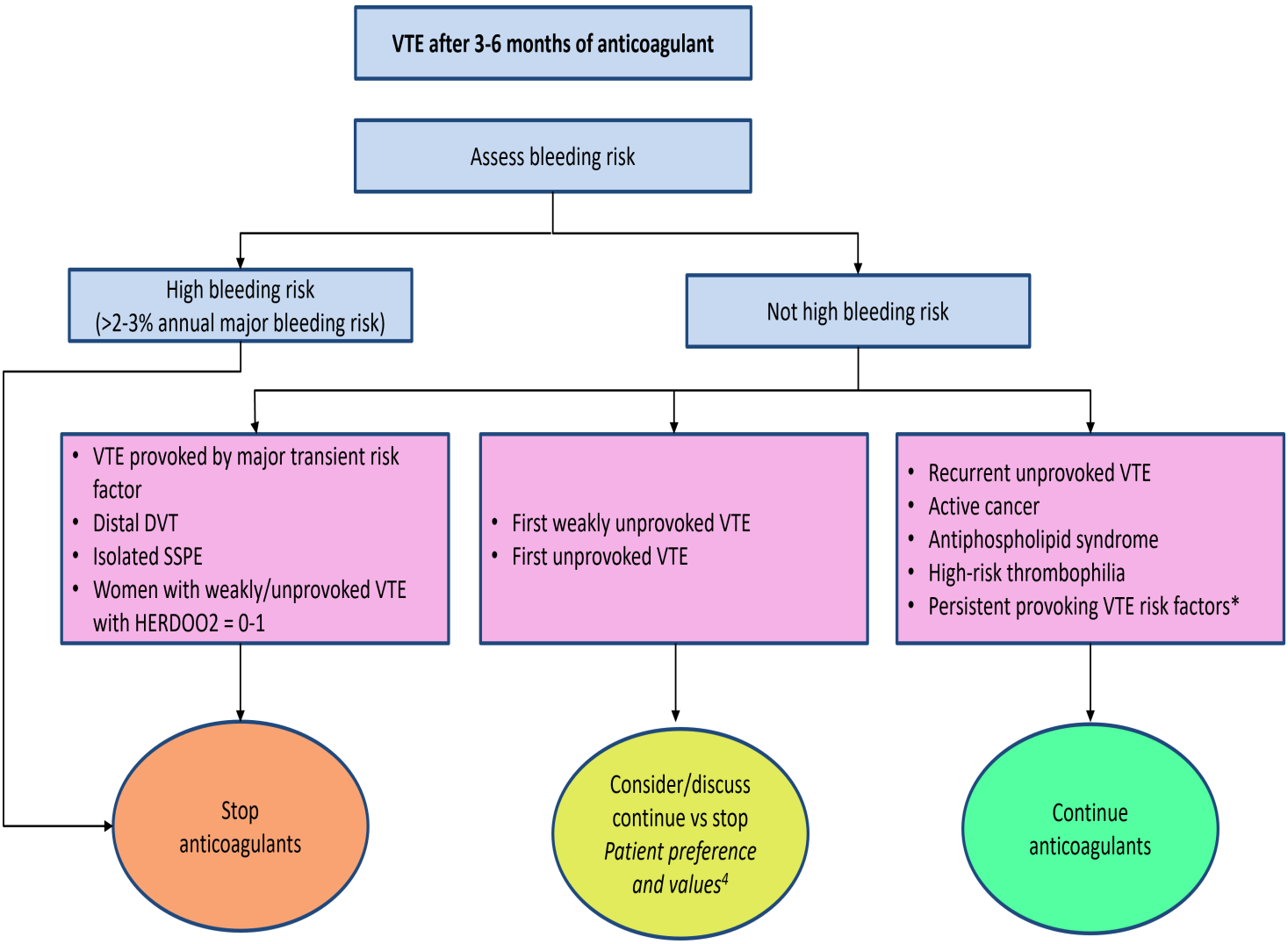
Background:

Determining the duration of anticoagulant therapy beyond the initial 3-6 month acute treatment period requires an individualized assessment of the ***risk of recurrent VTE after anticoagulation is stopped, the risk of major bleeding while on anticoagulation and the clinical consequences of each event.***

Consequences of Recurrent VTE and Consequences of Major Bleed

During the initial (acute) 3-6 months of VTE treatment, the case-fatality rate of recurrent VTE and major bleeding are similar. However, after completion of this initial treatment period, the case fatality rate associated with recurrent VTE during the secondary prevention phase is approximately 2-3 fold lower than that of major bleeding. Consequently, as outlined below, **patients with a high risk of bleeding (higher than 2-3% per year) are unlikely to benefit from extended or indefinite anticoagulation for secondary VTE prevention, irrespective of their estimated risk of recurrent VTE (see Figure 1).**

Figure 1. Continue or stop anticoagulants after initial 3-6 months of treatment for acute VTE



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Stop Anticoagulants in Patients at High Bleeding Risk (higher than 2-3% per year) Regardless of Recurrent VTE Risk

The risk of anticoagulant-associated bleeding is highest during the first 3 months of treatment and stabilizes after the first year.

Definitions of major bleeding vary across studies. However, contemporary studies usually define it as bleeding that is fatal, occurs in a critical organ/space, results in a reduction of hemoglobin of at least 20 g/L, and/or results in the transfusion of at least 2 units of blood.

Several bleeding risk scores, initially developed for patients with atrial fibrillation (AF) (e.g., HASBLED) or to predict early bleeding in patients with VTE (e.g., VTE Bleed or modified Riete or modified ACCP score), have recently been validated. The CHAP score was specifically developed for VTE patients but has not yet been validated. The modified ACCP score, modified Riete score, VTE-Bleed score and HASBLED score all help ***identify patients with high bleeding risk (2-3% annual major bleed risk) in whom anticoagulation should be discontinued regardless of the estimated risk of recurrent VTE.***

Almost all of these bleeding risk scores use the same predictors of bleeding (**see Table 1)**. Patients with two or more such risk factors are considered to be at high risk of bleeding and should stop anticoagulants.

TABLE 1: BLEEDING RISK FACTORS

- Age > 65
- Anemia (Hgb <100)
- Antiplatelet therapy use
- Chronic kidney disease (CrCl <50 ml/min)
- Prior history of major bleeding
- Thrombocytopenia (Ptls <50)

It is important to recognize that long term use of direct oral anticoagulants (DOACs) is safer than vitamin K antagonists (e.g., warfarin) with comparable VTE risk reduction.

Reduced-dose DOAC regimens have recently been studied to determine whether they preserve the efficacy of standard-dose DOACs while lowering bleeding risk during secondary VTE prevention. In the RENOVE study, patients who had completed at least 6 months of anticoagulation and required extended therapy were assigned to either reduced-dose (apixaban 2.5 mg bid or rivaroxaban 10 mg daily) or standard-dose DOAC. Rates of recurrent VTE remained very low and similar between groups (~2% over 5 years), while clinically relevant bleeding was lower with reduced-dose therapy. Accordingly, when extended anticoagulation is indicated, reduced dose DOACs should be offered.

In practice, assessment of major bleeding risk is primordial. As discussed above, patients with a high major bleeding risk (>2-3% per year) should discontinue anticoagulation (see **Figure 1**). For patients in whom anticoagulation is continued, ***reduced-dose DOACS are the preferred agents*** with limited exceptions (e.g., vitamin K antagonists when DOACs are contraindicated [triple-positive antiphospholipid antibody syndrome, etc.]).

Who is at High Enough Recurrent VTE Risk to Continue or Consider Continuing Anticoagulants?

The risk of recurrent VTE after stopping anticoagulation is similar whether anticoagulant therapy is stopped after 3-6 months or after 12-24 months of treatment. This suggests that 3-6 months of anticoagulation is sufficient to treat the acute episode of VTE when the decision is made not to continue long-term therapy. In contrast, shortening the duration of anticoagulation to 4 or 6 weeks is associated with an approximate doubling of the risk of recurrent VTE during the first 6 months after treatment cessation. Hence, 3-6 months represents the minimum recommended duration of anticoagulant therapy.

Patients with ***distal DVT*** and ***SSPE*** have a low risk of recurrent VTE after completing 3 months of anticoagulants and ***should stop anticoagulants at 3 months***.

In patients with proximal DVT and/or PE, a decision regarding continuation of anticoagulation beyond 3-6 months is required. This decision will depend on balancing the risk of recurrence with the risk of major bleeding. The risk of recurrent VTE depends mainly on whether the VTE was strongly provoked by a transient risk factor, weakly provoked by a transient risk factor, unprovoked, or related to a major persistent risk factor such as active cancer, ongoing inflammation, or ongoing immobility.

Patients with VTE Provoked by a Transient Risk Factor

Patients with VTE provoked by a major transient risk factor which has resolved should receive only 3 months of anticoagulation, as their risk of recurrent VTE after treatment discontinuation is less than 3% in the subsequent year. Patients with weakly provoked VTE, unprovoked VTE, or VTE associated with a persistent risk factor have higher risk of recurrent VTE and should undergo individualized discussion regarding continuation of anticoagulants beyond three months (see **Table 2** and **Figure 1**).

Table 2: Examples of Transient VTE Risk Factors

CATEGORY OF TRANSIENT RISK FACTOR	EXAMPLES OF RISK FACTORS
Major (in last 3 months)	• Surgery with general anesthetic for ≥30 minutes • Admission to hospital for an acute illness with confinement to bed for at least 3 days • Trauma with ER visit • Paster case immobilization
Minor (in last 3 months)	• Surgery with general anesthetic for <30 minutes • Admission to hospital with an acute illness for less than 3 days • Confined to bed out of hospital for at least 3 days with an acute illness • Hormonal therapy • Pregnancy or the puerperium • Leg injury associated with reduced mobility for at least 3 days

The strength of a reversible provoking risk factor is inversely related to the risk of recurrent VTE after discontinuation of anticoagulant therapy. As shown in **Table 3**, the risk of recurrence is lower for VTE provoked by a surgical (i.e., major) risk factor than for those associated with non-surgical (i.e., minor) risk factors. For both categories, the risk of recurrence is lower than observed after an unprovoked VTE or VTE associated with a strong persistent risk factor. It is also important to note that the more recent the exposure to transient risk factor, the stronger the association of that risk factor with the VTE and the lower the risk of recurrence after stopping anticoagulants. For example, a DVT 2 days after major surgery is more likely related to the major surgery than a DVT that occurs 3 months after major surgery and the risk of recurrence off anticoagulants will be lower in the former than the latter.

Table 3: Estimated Risk of Recurrence After Stopping Anticoagulation for a First VTE

	1 Year after Stopping Anticoagulants	5 Years after Stopping Anticoagulants
Surgical/Major	1-2%	3%
Non-surgical/Minor (e.g., hospitalization, plaster cast immobilization, hormonal therapy*, flight of > 8 hours, medical illness with immobilization)	5%	15%

*The risk of recurrence in women with a first VTE associated with estrogen-containing contraceptive use (4% by 5 years off anticoagulation) may be lower than that seen with VTE provoked by other minor risk factors.

Patients with Weakly or Unprovoked VTE:

Patients with a first episode of weakly provoked or unprovoked VTE should receive at least 3-6 months of anticoagulation. Decision regarding continuation of anticoagulation beyond this period should be individualized, based on the estimated risk of recurrence, bleeding risk, and patient preferences and values. For patients receiving extended therapy beyond 3 months, the decision should be revisited annually to reassess major bleeding risk (with discontinuation if the risk exceeds 2-3%), review patient preferences and values, and account for evolving comorbidities. In patients with a first weakly or unprovoked VTE, the choice between discontinuing anticoagulation and continuing therapy indefinitely is strongly influenced by the preferences of an **informed patient**. Engaging patients in understanding their individualized risks and benefits is essential. To elicit patient preferences for the purpose of joint decision-making, the expected risks of recurrence with and without indefinite anticoagulant therapy and the expected consequences of recurrent VTE and bleeding must be shared with the patient and understood by the patient.

On average, patients with a **first weakly or unprovoked episode of proximal DVT or pulmonary embolism (PE)** have a risk of recurrence of about 10% in the first year, 25% within 5 years and 36% within 10 years after stopping anticoagulant therapy. As shown in Table 4, the risk of recurrence is further modified by a patient sex.

Table 4: Estimated Risk of Recurrence after Stopping Anticoagulation Following an Unprovoked VTE

Gender	1 year after stopping anticoagulant(s)	5 years after stopping anticoagulant(s)
Males	11.9%	28.6%
Females	8.9%	21.2%

Prognostic models:

Prognostic models can help further identify subgroups of weakly or unprovoked VTE with risks low enough to safely stop anticoagulation.

Three models to predict the risk of recurrent VTE after anticoagulation discontinuation following a **first weakly or unprovoked DVT or PE** have undergone validation (i.e., in a patient population or data set separate from which they were derived). Only the HERDOO2 score has been prospectively validated (the highest standard of validation) while the other scores have only been retrospectively validated.

HERDOO2

Predictors of Recurrence	Rule
• Hyperpigmentation, edema or redness in either leg • VIDAS D-dimer ≥250 ug/L during anticoagulation • Body mass index (BMI) ≥30 kg/m^2 • Age ≥65 years	• Female patients with <2 predictors of recurrence have a low risk of recurrence (3.0% per patient year) and should stop anticoagulants • Women with ≥2 predictors of recurrence and all men are classified as high risk of recurrence and should discuss/consider continuing anticoagulants

The HERDOO2 score was developed and validated in a population with weakly and unprovoked VTE. Patients with strongly provoked VTE who should discontinue anticoagulation, and patients with cancer-associated VTE who should continue anticoagulation as long as the cancer is active, were excluded. Weakly provoked VTE included estrogen- and pregnancy-associated VTE. The HERDOO2 rule was derived and validated using the VIDAS D-dimer assay. Importantly, the D-dimer cut-point used in the HERDOO2 score is assay-specific and is set at half the threshold commonly used in the diagnostic algorithms for suspected VTE (250 ug/dl [HERDOO2 threshold] vs 500 ug/dl [diagnostic threshold]).

DASH

Predictors of Recurrence	Rule
• Abnormal D-dimer level after approximately 1 month off anticoagulation (+2 points) • Male sex (+1 point) • Age <65 years (+1 point) • Hormone use at VTE diagnosis (-2 points)	Those with a DASH score of ≤1 have a risk of recurrence of 3.5% per year

It should be noted that in patients older than 65 years, the risk of recurrent VTE was >5% even among those with the lowest DASH score. The clinical utility of the DASH score in men is limited as almost all men have a DASH score of higher than 1. It is also important to acknowledge that the use of the DASH score also requires temporary discontinuation of anticoagulation for one month to allow for D-Dimer testing. This period coincides with the time for highest risk for VTE recurrence after stopping therapy, thereby exposing patients to increased risk and limiting the practicality of routine DASH score use.

The **Vienna Prediction Model**, which includes sex, site of index event and D-dimer, uses a nomogram to estimate the risk of VTE recurrence at 1 year and 12 years after discontinuation of anticoagulation. This model demonstrated suboptimal performance in prospective validation. In a prospective cohort study,

patients classified as low risk still experience recurrent VTE at a rate of 5.2% at 1 year, and 11.2% at 2 years after stopping anticoagulant therapy. Similarly, a randomized controlled trial (RCT) comparing Vienna Prediction Model-guided management with usual care showed that use of the model did not reduce the risk of recurrent VTE.

Patients with Persistent Risk Factors:

Patients with strong, persistent risk factors (active cancer, high-risk thrombophilia) should remain on anticoagulation indefinitely if the bleeding risk is acceptable (i.e., non-high bleeding risk <2-3% per year).

1. **Persistent risk factors that usually prompt continuation of anticoagulation:**
    - **Active cancer:** The risk of recurrent VTE is markedly increased in patients with active cancer. This risk is higher in patients with metastatic disease (compared with localized disease) and in patients receiving chemotherapy. [See **Clinical Guide:** Cancer and Thrombosis]
    - **Antiphospholipid antibody positivity:** The presence of persistently positive moderate-to-high titer antiphospholipid antibodies and/or a lupus anticoagulant and VTE or arterial thrombosis (fitting the criteria for antiphospholipid syndrome) is considered high risk for VTE recurrence (and arterial thrombosis), and these patients should generally receive anticoagulant therapy indefinitely. Consultation with a Thrombosis specialist or Hematologist is suggested especially in triple positive anti-phospholipid antibody patients who may need vitamin K antagonists. [See **Clinical Guide:** Thrombophilia: Antiphospholipid Syndrome]
    - **High risk hereditary thrombophilia**: Patients with antithrombin, protein C or protein S deficiency or who are homozygous or compound heterozygous for factor V Leiden and/or prothrombin G20210A with a history of VTE have a high risk of recurrent VTE. These patients may be candidates for indefinite anticoagulant therapy. Consultation with a Thrombosis specialist or Hematologist is suggested to complete thrombophilia testing in patients with weakly provoked or unprovoked VTE. [See **Clinical Guides:** Thrombophilia: Deficiencies in Protein C, Protein S, and Antithrombin **and** Thrombophilia: Factor V Leiden and Prothrombin Gene Mutation]
    -
2. **Persistent risk factors that do not usually influence the duration of anticoagulation**:
    - **Low risk hereditary thrombophilia and/or family history of VTE:** The presence of common low-risk hereditary thrombophilias (i.e., heterozygosity for factor V Leiden or prothrombin G20210A) does not appear to be a clinically important risk factor for recurrence of VTE either during or after anticoagulant therapy. A positive family history alone does not increase the risk of recurrent VTE.
    - **Presence of an inferior vena cava filter:** The presence of an inferior vena cava filter alone should not determine the duration of anticoagulant therapy beyond the duration of treatment for the VTE that triggered the filter insertion. IVC filter thrombosis rates are high in patients with cancer, and continued anticoagulation is generally required in this setting.
    - **Residual abnormalities on ultrasound**: Residual vein obstruction on follow-up ultrasound is detected in approximately one-half of patients. Although these findings may slightly increase the likelihood of recurrence after stopping anticoagulants, the associated risk is insufficient for residual vein obstruction alone to guide decisions regarding duration of anticoagulant therapy.

Recent evidence from an RCT evaluating reduced dose apixaban for extended treatment of VTE provides important insights into the management of patients with provoked VTE with ongoing comorbidities (e.g., persistent immobility, obesity, heart failure, chronic lung disease, chronic kidney disease, chronic inflammatory or autoimmune disease, chronic infection, or atherosclerotic cardiovascular disease). Reduced-dose apixaban resulted in a substantially greater absolute reduction in recurrent VTE among patients without atherosclerotic cardiovascular disease, with minimal major bleeding, supporting continued anticoagulation in this group. In contrast, patients with cardiovascular disease as the ongoing comorbidity derived a much smaller absolute benefit from extended anticoagulation. In this latter group, long-term aspirin therapy may be a reasonable alternative for ongoing secondary VTE prevention and arterial event secondary prevention.

Patients with a Second Episode of VTE

Although a second episode of VTE suggests a higher risk of recurrence, the recommendation for duration of anticoagulant therapy is dependent on provoking factors (**see Figure 1**).

Summary and Practical Decision Framework

Decisions regarding extended anticoagulation should integrate the estimated risk of recurrent VTE, the risk of bleeding, and patient values and preferences (see **Figure 1**). Anticoagulation can be safely discontinued in patients with VTE provoked by a major transient risk factor, patients with distal DVT, patients with SSPE, and women with weakly or unprovoked VTE classified as low risk using the HERDOO2 rule. Extended anticoagulation is generally recommended for patients with persistent risk factors (e.g., cancer, ongoing immobility, antiphospholipid syndrome, high-risk thrombophilia) and for those with recurrent unprovoked VTE.

Patients with a first weakly or unprovoked VTE often fall into a preference-sensitive zone where net harm or benefits are very marginal, highlighting the importance of sharing absolute long-term risks of recurrent VTE and bleeding and helping patients make informed decisions. Reduced-dose DOACs provide similar protection against recurrent VTE with lower bleeding risk and are the treatment of choice for those continuing anticoagulants. When discontinuing therapy, clinicians should ensure that patients understand symptoms of recurrence, when to seek medical attention, and how changes in clinical status or new risk factors may modify future risk.

Special Considerations:

Pediatrics

If possible, pediatric hematologists with experience in thromboembolism should manage children with or at risk for thrombosis, as well as those receiving antithrombotic therapy. When this is not possible, a combination of a neonatologist/pediatrician and an adult hematologist, supported by consultation with an experienced pediatric hematologist, should manage these children. Duration recommendations in pediatric populations remain individualized; evidence for extended DOAC therapy in adolescents is emerging but limited.

Central venous catheter (CVC) associated VTE

CVC-associated VTE should be treated like a provoked VTE. [See **Clinical Guide: Central Venous Catheter-Related Thrombosis**].

Relevant Thrombosis Canada Clinical Guides:

- Apixaban (Eliquis®)
- Cancer and Thrombosis
- Central Venous Catheter-Related Venous Thrombosis
- Deep Vein Thrombosis (DVT): Treatment
- Pregnancy: Venous Thromboembolism Treatment
- Pulmonary Embolism (PE): Treatment
- Rivaroxaban (Xarelto®)
- Thrombophilia: Antiphospholipid Antibody Syndrome
- Thrombophilia: Deficiencies in Protein C, Protein S, and Antithrombin
- Thrombophilia: Factor V Leiden and Prothrombin Gene Mutation

Relevant Thrombosis Canada Patient Materials:

- Choosing an Anticoagulant
- When Can I Stop My Anticoagulant?

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References:

Agnelli G, et al. Apixaban for extended treatment of venous thromboembolism. N Engl J Med 2013;21;368(8):699-708.

Carrier M, et al. Systematic review: case-fatality rates of recurrent venous thromboembolism and major bleeding events among patients treated for venous thromboembolism. Ann Intern Med 2010;152(9):578-589.

Couturaud F, et al. Extended treatment of venous thromboembolism with reduced-dose versus full-dose direct oral anticoagulants in patients at high risk of recurrence: a non-inferiority, multicentre, randomised, open-label, blinded endpoint trial. Lancet 2025;405(10480):725-735.

Eichinger S, et al. Risk assessment of recurrence in patients with unprovoked deep vein thrombosis or pulmonary embolism: the Vienna prediction model. Circulation 2010;121:1630-1636.

Eischer L, et al. The risk of recurrence in women with venous thromboembolism while using estrogens: a prospective cohort study. J Thromb Haemost 2014;12:635-640.

Ensor J, et al. Systematic review of prognostic models for recurrent venous thromboembolism (VTE) post-treatment of first unprovoked VTE. BMJ Open 2016;6(5):e01190.

Geersing GJ, et al. Effect of tailoring anticoagulant treatment duration by applying a recurrence risk prediction model in patients with venous thromboembolism compared to usual care: a randomized controlled trial. PLoS Med 2020;17(6):e1003142.

Le Gal G, et al, SSPE Investigators. Risk for recurrent venous thromboembolism in patients with subsegmental pulmonary embolism managed without anticoagulation: a multicenter prospective cohort study. Ann Intern Med 2022;175(1):29–35.

Kearon C, 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. Chest 2016;149(2):315-352.

Kearon C, et al. Categorization of patients as having provoked or unprovoked venous thromboembolism: guidance from the SSC of ISTH. J Thromb Haemost 2016:14:1480-1483.

Kearon C, et al. Long-term risk of recurrence in patients with a first unprovoked venous thromboembolism managed according to D-dimer results: a cohort study. J Thromb Haemost 2019;17(7):1144-1152.

Khan F, et al. Long term risk of symptomatic recurrent venous thromboembolism after discontinuation of anticoagulant treatment for first unprovoked venous thromboembolism event: systematic review and meta-analysis. BMJ 2019;366:14363.

Khan F, et al. Long-term risk for major bleeding during extended oral anticoagulant therapy for first unprovoked venous thromboembolism: a systematic review and meta-analysis. Ann Intern Med 2021;174:1420-1429.

Kyrle PA, et al. The Vienna Prediction Model for identifying patients at low risk of recurrent venous thromboembolism: a prospective cohort study. Eur Heart J 2024;45(1):45–53.

Marcucci M, et al. Risk of recurrence after a first unprovoked venous thromboembolism: external validation of the Vienna Prediction Model with pooled individual patient data. J Thromb Haemost 2015;13:775-781.

Piazza G, et al. Apixaban for extended treatment of provoked venous thromboembolism. N Engl J Med. 2025;393(12):1166-1176.

Rodger MA, Le Gal G. Who should get long-term anticoagulant therapy for venous thromboembolism and with what? Blood Adv 2018;2(21):3081-3087.

Rodger MA, et al. REVERSE II Study Investigators. Validating the HERDOO2 rule to guide treatment duration for women with unprovoked venous thrombosis: multinational prospective cohort management study. BMJ 2017;356:j1065.

Rodger MA, et al. REVERSE II Investigators. "HERDOO2" clinical decision rule to guide duration of anticoagulation in women with unprovoked venous thromboembolism. Can I use any d-Dimer? Thromb Res 2018;169:82-86.

Streiff MB, et al. Guidance for the treatment of deep vein thrombosis and pulmonary embolism. J Thromb Thrombolysis 2016;41(1):32-67.

Stevens SM, et al. Antithrombotic therapy for VTE disease: compendium and review of CHEST Guidelines 2012-2021. Chest. 2024;166(2):388-404.

Tosetto A, et al. External validation of the DASH prediction rule: a retrospective cohort study. J Thromb Haemost 2017;15:1-8.

Weitz J, et al. Rivaroxaban or aspirin for extended treatment of venous thromboembolism. N Engl J Med 2017; 376(13):1211-1222.

Wells et al, Predicting major bleeding during extended anticoagulation for unprovoked or weakly provoked venous thromboembolism. Blood Advances 2022;6(15):4605-4616.

Wu C, et al. Case-fatality of recurrent venous thromboembolism and major bleeding associated with aspirin, warfarin, and direct oral anticoagulants for secondary prevention. Thromb Res 2015;135(2):243-248.

Yamashita Y, et al. ONCO DVT Study Investigators. Edoxaban for 12 months versus 3 months in patients with cancer with isolated distal deep vein thrombosis (ONCO DVT study): An open-label, multicenter, randomized clinical trial. Circulation. 2023;148(21):1665-1676.

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