

# EVIDENCE BASED STATEMENT

DOMAIN **06**, Statement **10**

TOPIC: “**DOACs use in acute venous thrombo-embolism management**”

## SEARCH TERMS & SOURCES

("venous thrombosis" OR "venous thromboembolism" OR "VTE" OR "DVT") AND ("DOAC" OR "direct oral anticoagulant" OR "direct-acting oral anticoagulant" OR "direct thrombin inhibitor" OR "factor Xa inhibitor") AND ("treatment" OR "management") AND ("meta analysis" OR "systematic review" OR "guidelines")

## INCLUSION CRITERIA

Systematic review or meta-analysis (2012-2022)  
Focused on anticoagulation for VTE  
Last five years

## SEARCH RESULT BEFORE - AFTER SELECTION

179 – 20

## PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Kakkos SK, Gohel M, Baekgaard N, et al. European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis 5.
2. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608.
3. Mazzolai L, Ageno W, Alatri A, et al. Second consensus document on diagnosis and management of acute deep vein thrombosis: updated document elaborated by the ESC Working Group on aorta and peripheral vascular diseases and the ESC Working Group on pulmonary circulation and right ventricular function. European Journal of Preventive Cardiology. 2021 Jul 13.
4. Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood advances. 2020 Oct 13;4(19):4693-738.
5. Diaconu N. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). European Heart Journal. 2020 Jan 21;41(4):543-603.
6. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016 Feb 1;149(2):315-52.

# EVIDENCE BASED STATEMENT

## Domain 6; Statement 10

### IDENTIFIED REFERENCES

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2. Ueyama H, Miyashita H, Takagi H, et al. Network meta-analysis of anticoagulation strategies for venous thromboembolism in patients with cancer. *J Thromb Thrombolysis.* 2021 Jan;51(1):102-111. doi: 10.1007/s11239-020-02151-2. PMID: 32458316.
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5. Nugroho Eko Putranto J, Wardhana A, Noor YA, et al. Factor Xa inhibitor for venous thromboembolism management in patient with cancer: a systematic review and meta-analysis. *F1000Res.* 2021 Dec 8;10:1257. doi: 10.12688/f1000research.73883.1. PMID: 35136585; PMCID: PMC8802150.
6. Nisly SA, Mihm AE, Gillette C, et al. Safety of direct oral anticoagulants in patients with mild to moderate cirrhosis: a systematic review and meta-analysis. *J Thromb Thrombolysis.* 2021 Oct;52(3):817-827. doi: 10.1007/s11239-021-02424-4. Epub 2021 Mar 16. PMID: 33728575.
7. Murphy AC, Koshy AN, Farouque O, et al. Factor Xa Inhibition for the Treatment of Venous Thromboembolism Associated With Cancer: A Meta-Analysis of the Randomised Controlled Trials. *Heart Lung Circ.* 2021 Dec 9:S1443-9506(21)01349-4. doi: 10.1016/j.hlc.2021.10.024. Epub ahead of print. PMID: 34896013.
8. Mohamed MFH, ElShafei MN, Ahmed MB, et al. The Net Clinical Benefit of Rivaroxaban Compared to Low-Molecular-Weight Heparin in the Treatment of Cancer-Associated Thrombosis: Systematic Review and Meta-Analysis. *Clin Appl Thromb Hemost.* 2021 Jan-Dec;27:1076029620940046. doi: 10.1177/1076029620940046. PMID: 33651658; PMCID: PMC7930650.
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12. Katel A, Aryal M, Neupane A, et al. Efficacy and Safety of Direct Oral Anticoagulants in Venous Thromboembolism Compared to Traditional Anticoagulants in Morbidly Obese Patients: A Systematic Review and Meta-Analysis. *Cureus.* 2021 Apr 20;13(4):e14572. doi: 10.7759/cureus.14572. PMID: 34026385; PMCID: PMC8135070.
13. Herold J, Bauersachs R. Comment on: Reduced dose direct oral anticoagulants (DOACs) in the extended treatment of venous thromboembolism: a systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis: JTH* 2018 Jul; 16(7): 1288-95. *J Thromb Haemost.* 2021 Sep;19(9):2357-2358. doi: 10.1111/jth.15426. PMID: 34435433.
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# EVIDENCE BASED STATEMENT

## Domain 6; Statement 10

### TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 06, Statement 04, TOPIC: “**DOACs use in acute venous thrombo-embolism management**”

DOACs have been shown to have significantly lower rates of major bleeding compared to vitamin K antagonists or LMWH (RR 0.61, 95% CI 0.45 – 0.83) (Kakkos SK, Gohel M, Baekgaard N, et al. **European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis**). For patients with unprovoked VTE, extended treatment with DOACs results in VTE recurrence rates superior comparable to vitamin K antagonists (Stevens SM, Woller SC, Kreuziger LB, et al. **Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608**). Because these agents are dosed orally once a day and do not require laboratory monitoring, they also have the advantage of being easier for patients to manage. Consequently, they are now widely recommended as first line pharmacotherapy for acute DVT and PE (Kakkos SK, Gohel M, Baekgaard N, et al. **European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis; Stevens et al. 2021**). Prior to starting DOACs, it is always important to evaluate patient renal function and to consider possible drug interactions. Patients with unprovoked VTE should be treated with extended DOAC therapy unless bleeding risk is prohibitive. Risk factors for major bleeding on DOACs include age greater than 65, creatinine clearance below 50 mL/min, a history of bleeding, use of antiplatelet therapy, and hemoglobin level less than 100 g/L (Stevens SM, Woller SC, Kreuziger LB, Bounameaux H, et al. **Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608**).

Because of the safety profile and ease of administration, DOACs have helped to usher in a shift towards outpatient treatment of DVT. Guidelines recommend outpatient treatment of DVT with DOACs with the following exceptions: patients at risk of massive PE, massive or recurrent VTE, pregnancy, and lack of access to care and social support (Kakkos SK, Gohel M, Baekgaard N, et al. **European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis**). Published evidence now favors the safety of outpatient management for patients with low-risk PE as well, provided they meet the above criteria (Stevens et al. 2021).

Meta analyses of cancer patients with VTE suggest that DOACs may lead to lower rates of VTE recurrence than LMWH (RR 0.65, 95% CI 0.42–1.01). Meta analyses differ as to whether DOACs have a similar or slightly higher rate of clinically significant bleeding than LMWH. Regardless, the risk of bleeding is still significant and cancer patients at risk of bleeding should have a careful consideration of risks and benefits before starting DOAC therapy (Lyman GH, Carrier M, Ay C, et al. **American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. Blood Adv. 2021 Feb 23;5(4):927-974**).

# EVIDENCE BASED STATEMENT

## Domain 6; Statement 10

### STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 06, Statement 10

Direct oral anticoagulants (DOAC) is the first-line options for most adults for venous thrombo-embolism treatment. Before starting a DOAC, a thorough laboratory workup, including tests for kidney function, should be performed.

### 4 SELECTED REFERENCES

1. Kakkos SK, Gohel M, Baekgaard N, et al. European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis
2. Stevens SM, Woller SC, Kreuziger LB, Bounameaux H, Doerschug K, Geersing GJ, Huisman MV, Kearon C, King CS, Knighton AJ, Lake E. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. *Chest*. 2021 Dec 1;160(6):e545-608.
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### identified LITERATURE BIAS

Minimal due to large number of RCTs and meta analyses comparing DOACs to other forms of anticoagulation for treatment of VTE.

### SUGGESTED NEXT LINES OF RESEARCH

Clinical trials comparing different DOACs to determine the safest and most effective treatments for VTE.